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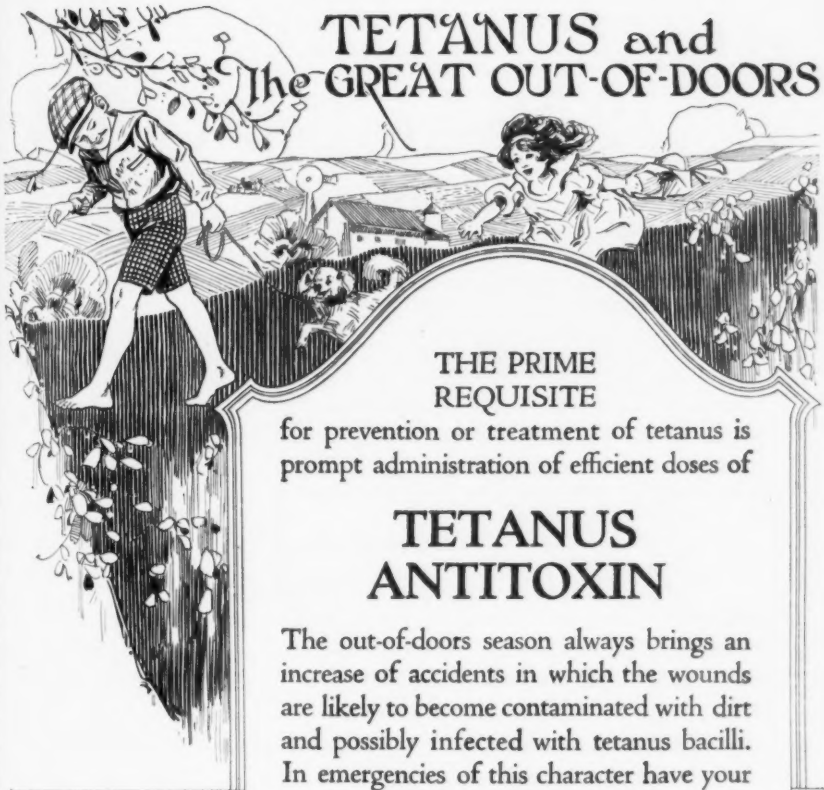

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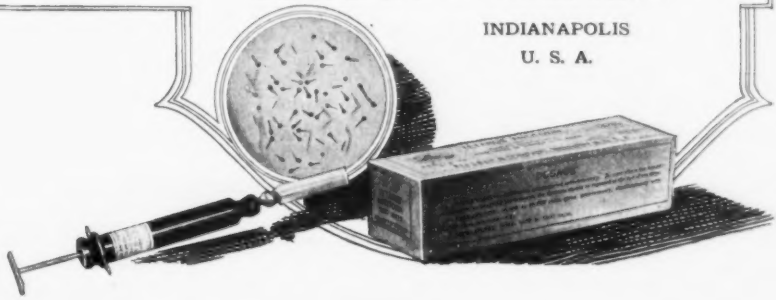

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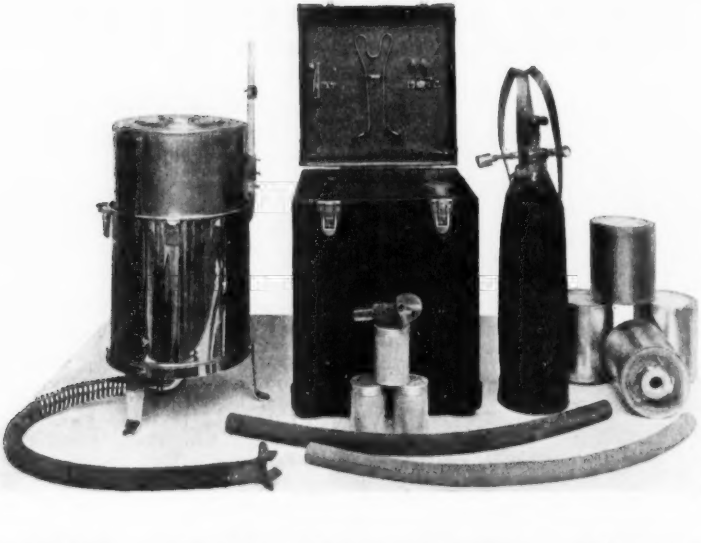

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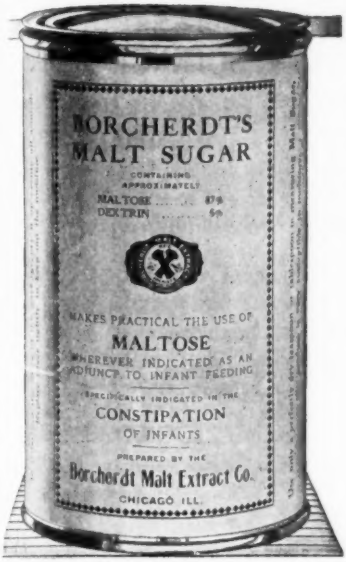

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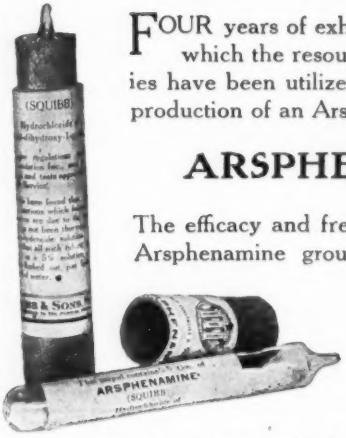

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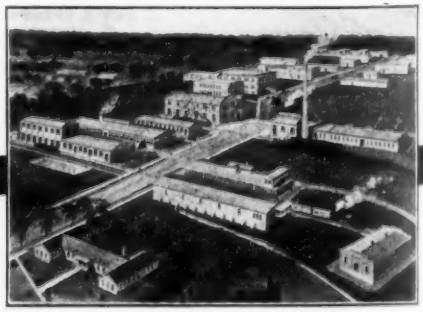

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ORIGINAL ARTICLES.

THE BREATHING OF AIR OF LOWERED OXYGEN TENSION AS A TEST OF CIRCULATORY FUNCTION.

By Alfred Stengel, M.D., Charles C. Wolferth, M.D.,

and

Leon Jonas, M.D.,[1]

Philadelphia, Pa.

(From the Medical Division of the Hospital of the University of Pennsylvania and the William Pepper Laboratory of Clinical Medicine of the University of Pennsylvania.)

Henderson and his co-workers[2] [3] have recently reported favorably on the value of gradual lowering of oxygen tension of respired air by means of a rebreathing apparatus as a test of cardiac function. While these workers speak of the test as one of cardiac function, it is apparent that the work of the heart alone, in the adaptation to anoxemia cannot be separated from that of the circulatory function as a whole.

The response to anoxemia involves a number of body mechanisms, the relative importance of which has not been definitely settled. Gregg, Lutz and Schneider[4] state that individuals differ in their responses to low oxygen tension, pointing out that some compensate

[1] Woodward Fellow in Physiological Chemistry, William Pepper Laboratory of Clinical Medicine, University of Pennsylvania.

[2] Jour. Am. Med. Assn., 1918, lxxi, 1382. Schneider, E. C.: Jour. Am. Med. Assn., 1918, lxxi, 1384. Whitney, J. L.: Jour. Am. Med. Assn., 1918, lxxii, 1389.

[3] Air Service Medical, Washington, D. C., 1919.

[4] Am. Jour. Physiol., 1919, l, 216.

largely by increased respiration, while others depend almost wholly on increased blood-flow. Haldane, Kellas and Kennaway,[5] on the other hand, hold that anoxemia cannot be compensated for by mere increase in breathing or circulation; the advantage gained by higher saturation of the blood with oxygen in the lungs is counteracted by the increased sweeping out of carbon dioxide which results in shifting of the dissociation curve for oxyhemoglobin. Owing to this, the hemoglobin combines more readily with oxygen in the lungs but holds on to it more tightly in the tissues, so that the supply is not much improved, although the blood is redder.

We have attempted to determine the usefulness of tests with the rebreathing apparatus for clinical purposes in hospital work, especially with respect to its value in estimating circulatory efficiency. We have made a number of studies on presumably normal individuals, also convalescent hospital patients who had no anemia, lung disease nor apparent circulatory deficiency, as well as a few patients with pneumokoniosis and a number with varying degrees of circulatory inadequacy. A great many of the tests were not satisfactory, as it is difficult to get patients from hospital wards and out-patient departments to coöperate perfectly in a procedure that gives them some inconvenience and sometimes unpleasant sensations. We have selected for presentation at this time, studies on a few cases with advanced disease; two with pneumokoniosis and five with either narrow margins of cardiac reserve or actual broken compensation. In all the hemoglobin percentage was 75 or more (Sahli). None showed any arrhythmia nor developed any during the test except occasional slight sinus arrhythmia coincident with increased breathing. The cases of pneumokoniosis were fairly well advanced in the so-called second stage. They were studied in the effort to learn to what extent pulmonary lesions of their type might be expected to interfere with the aëration of the blood while breathing air with lowered oxygen content.

Methods. A rebreathing apparatus was used similar to the one described by Henderson.[1] The volume of air used was an amount on which the subject, if he were normal, might be expected to reach the limit of this tolerance in about thirty minutes. Respiration rate, blood-pressure and pulse readings were taken for several minutes after the mask was adjusted, but before the actual test was begun. Notes were made on the clinical findings at this time. After the patient began breathing into the apparatus, blood-pressure readings and pulse-rate observations were noted every minute; frequent examinations of the heart were made and the general condition and the color noted.

Although the observers in the Air Service[5] have found psychological tests of extreme importance in the study of the reactions of

[5] Jour. Physiol., 1919, liii, 181.

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aviators, the tests described by them were scarcely practicable in individuals of the grade of intelligence found in hospital wards, many of whom are foreigners. We were compelled to resort to simple tests, such as affirmative or negative signs to questions. By this method we have avoided carrying any of our subjects to complete unconsciousness, but still have been able to test them close to the limit of psychic efficiency, where it manifested itself before physical distress.

Where feasible, exercise tests have been carried out with a Martin type of bicycle ergometer. Cardiac cases were usually tested with 6000 foot pounds of work in two minutes. Observations were made as with respect to any apparent distress or exhaustion, pulse reactions and dyspnea. Air breathed during the exercise and the next minute was collected in a Douglas bag and the quantity expired measured by an experimental gas meter. When the ergometer tests could not be carried out, observations were made on reactions to simple exercises such as stair-climbing.

SUMMARY OF CASES.

Case I.—I. W., white, male, aged forty-five years; coal miner.

Diagnosis. Osteo-arthritis of lumbar spine; second stage pneumokoniosis. The diagnosis of pneumokoniosis was made by *x*-ray. No evidence of cardiovascular disease. Only symptoms were those referable to the osteo-arthritis. Good response to lowered oxygen tension (Chart I).

Case II.—T. H., white, male, aged forty-nine years; potter.

Diagnosis. Pneumokoniosis, second stage; pulmonary emphysema; general vascular sclerosis; chronic constipation. Has been a potter for over thirty years and has had "potter's asthma" for many years. Becomes short of breath on exertion. *X*-ray showed second stage pneumokoniosis. Exercise tolerance fair. Performed work of 6000 foot pounds easily but with more than the usual hyperpnea. Good response to lowered oxygen tension (Chart II).

Case III.—J. N. H., white, male, aged twenty-seven years; laborer.

Diagnosis. Valvular heart disease (aortic stenosis and regurgitation, mitral regurgitation). History of rheumatic fever and repeated attacks of tonsillitis. Shortness of breath on climbing stairs or ladder. Palpitation especially at night interfering with sleep. Examination showed slight cyanosis of lips, ears and finger tips; very large heart with transverse measurement of 18 cm. and the signs of advanced disease of the aortic valve, and also mitral involvement. The response to 6000 foot pounds of exercise in two minutes on the bicycle ergometer was poor. He became exhausted, there

was hyperpnea and marked pulse reaction. Fairly good response to lowered oxygen tension (Chart III).

CASE IV.—A. O., white, male, aged thirty-two years; blacksmith's helper.

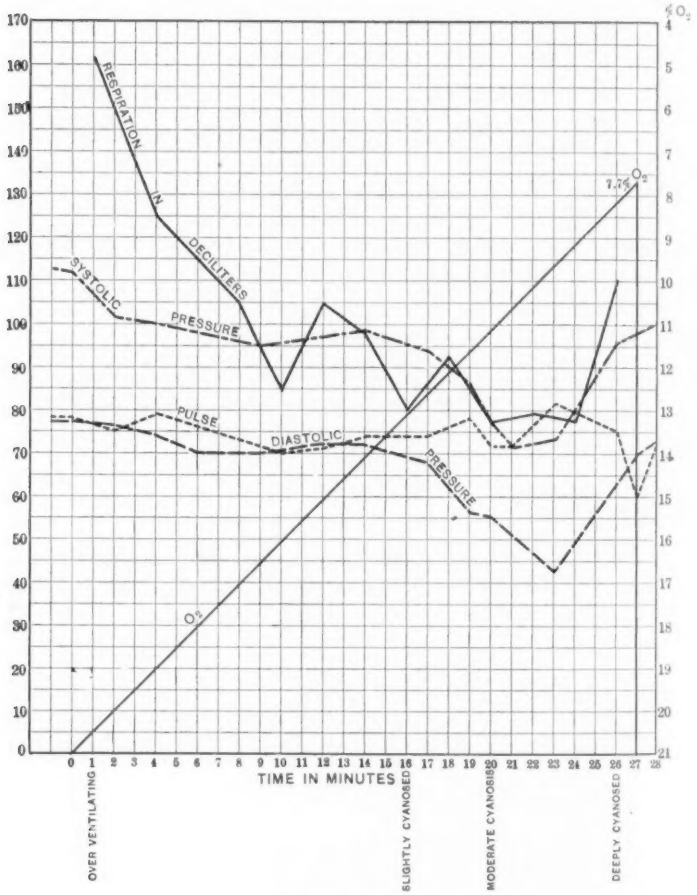

CHART I

Diagnosis. Valvular heart disease (mitral regurgitation); slight decompensation. History of rheumatic fever twelve years ago. Shortness of breath on exertion and palpitation; much worse recently. Cough for five weeks. Examination showed slight

cyanosis of lips, ears and finger tips, slight edema of ankles. Transverse measurement of cardiac area 17.5 cm. Moist rales at bases of both lungs. After ten days' rest, cyanosis, rales and edema disappeared. The rebreathing test done at this time showed fairly good response to lowered oxygen tension (Chart IV).

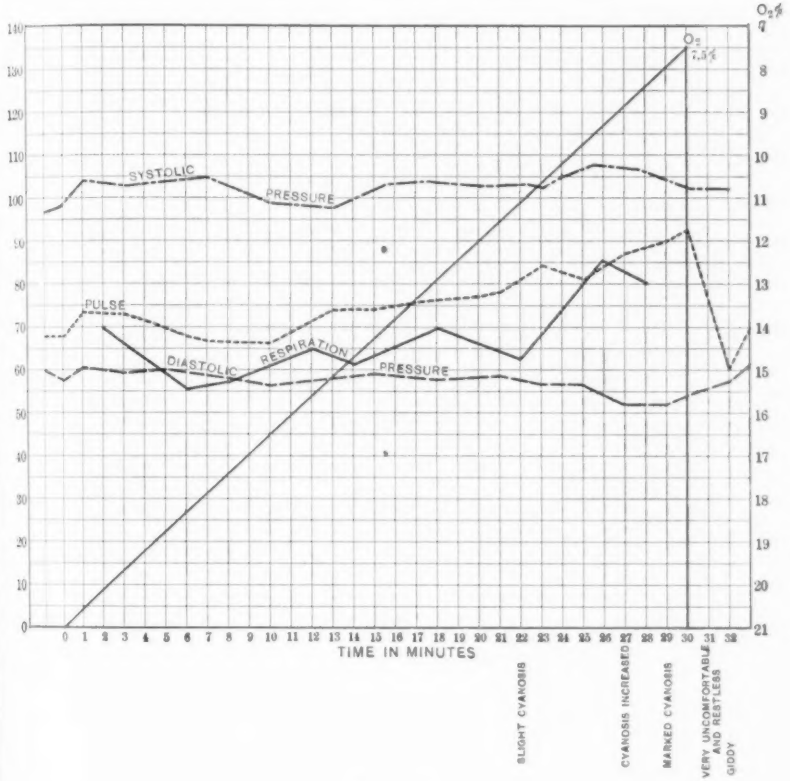

CHART II

CASE V.—J. O. N., white, male, aged forty-nine years; motorman. Diagnosis. Valvular heart disease (mitral stenosis); slight decompensation. Rheumatic fever twenty years ago. Recently, shortness of breath and palpitation on slight exertion; cough worse at night with occasional blood-tinged expectoration, and swelling of feet and legs if he stood much. Examination showed slight orthopnea, transverse cardiac measurement of 16.5 cm., presystolic thrill and murmur. Lungs were somewhat emphysematous, with many moist rales at both bases. The reaction to exercise was poor.

He was barely able to do 6000 foot pounds in two minutes on the ergometer. The dyspnea was quite marked but the pulse reaction was not excessive. The response in the rebreathing test was fairly good (Chart V).

CASE VI.—M. W., white, female, aged twenty-eight years; housewife.

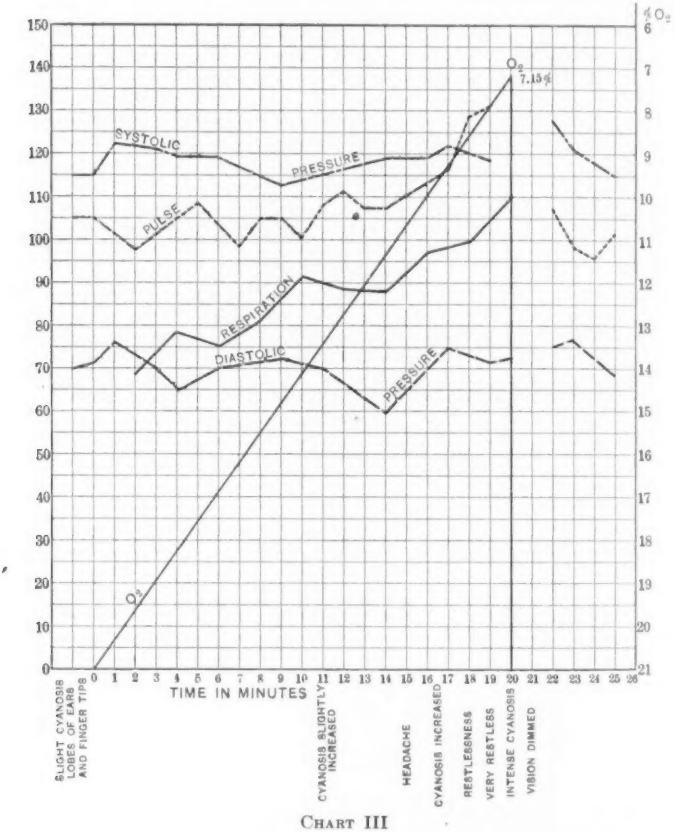

CHART III

Diagnosis. Valvular heart disease (mitral stenosis). History of attacks of rheumatic fever, nine and seven years ago. For the past three years acute attacks of weakness, shortness of breath and palpitation after exertion; recently had a very severe attack that kept her in bed several days. Examination showed the heart enlarged, with a transverse measurement of 14 cm. Presystolic thrill and murmur, accentuated pulmonic second sound. Few moist rales at

bases of both lungs. Pulse-rate unstable, usually normal in the morning, but frequently 100 to 115 in the afternoon. Tolerance to exercise very poor. Dyspnea and marked tachycardia, also a complaint of palpitation on climbing a flight of stairs. The response to lowered oxygen tension was poor (Chart VI).

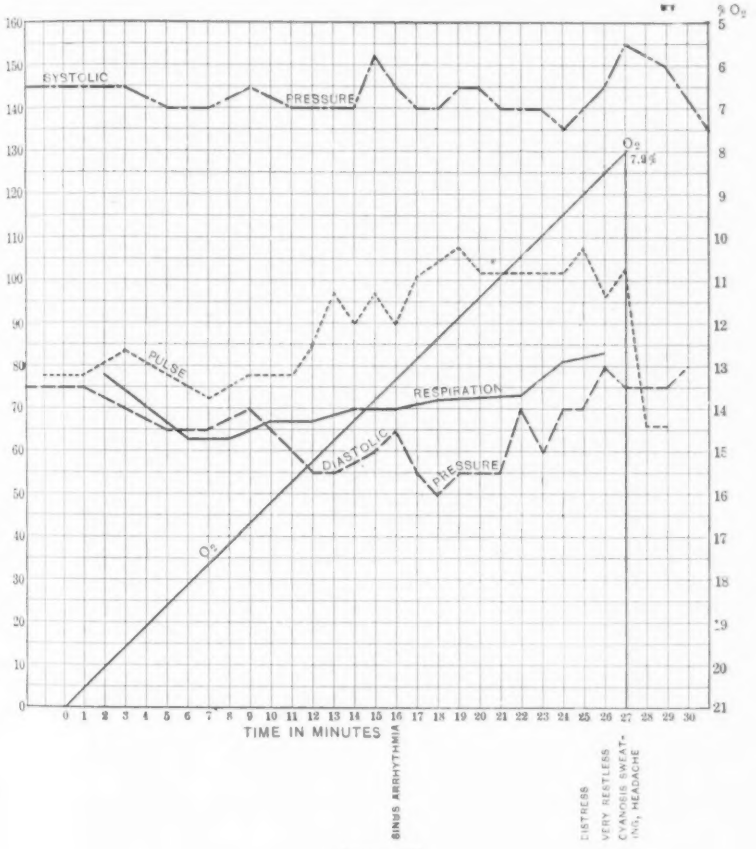

CHART IV

CASE VII.—F. M. B., white, male, aged twenty-seven years; printer.

Diagnosis. Valvular heart disease (mitral stenosis); cardiac decompensation. History of scarlet fever and repeated attacks of tonsillitis. Shortness of breath for three years, but three months ago it became so severe that he was unable to walk. Also had

palpitation and vertigo. Improved somewhat recently. Examination showed slight cyanosis of ears and finger tips. Heart enlarged; transverse measurement 16 cm. Presystolic thrill and murmur at apex. Many moist rales at the bases of both lungs. Liver extended three finger-breadths below the costal margin in the midclavicular line. Urine contained a cloud of albumin and

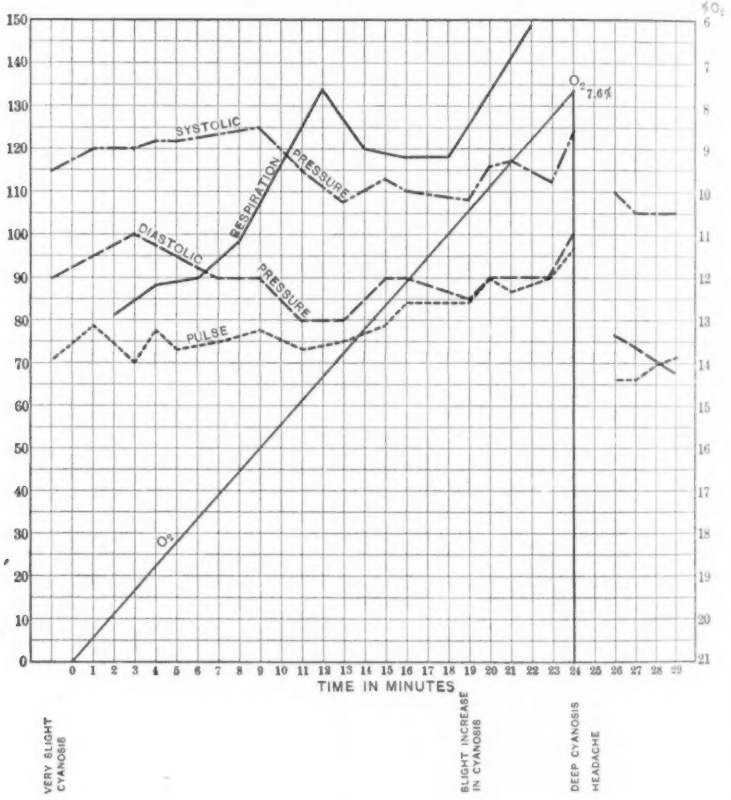

Chart V

many casts. Phthalein elimination 37 per cent. in two hours. The reaction to lowered tension of oxygen was poor (Chart VII).

Comment. In view of the comparatively slight respiratory increase that usually occurs in anoxemia, it was to be expected that moderately advanced pneumokoniosis would not interfere very materially with the ability of an individual to compensate for

low oxygen. This proved to be the case in two examples of this condition.

Some of the results in cardiac cases were unexpected. If the heart always played an important part in the compensation for anoxemia in all the cases presented, we should have expected an early breakdown in the rebreathing test. Early failure did indeed occur in two of the five cases—notably in the one with the most

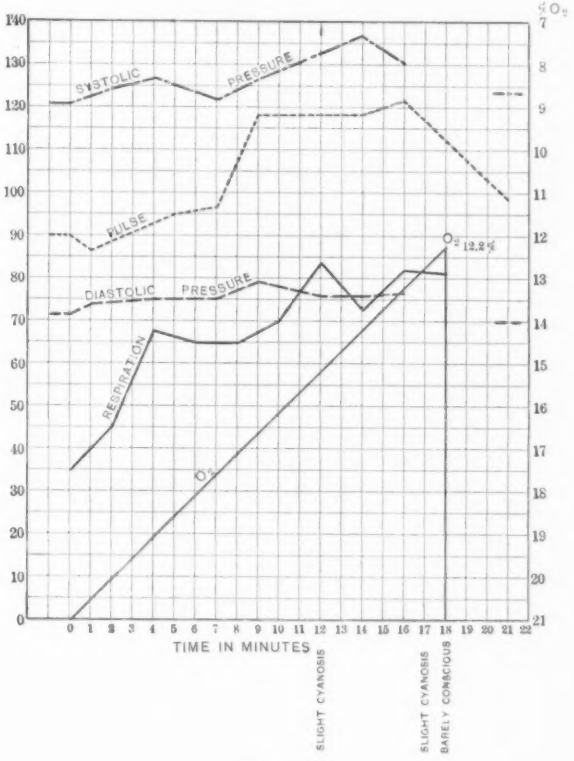

CHART VI

advanced decompensation (Case VII). In these two cases, apparently, demands were made on the circulation that could not be met. In the other three cases however, and notably in two with clinical evidences of broken compensation (Cases IV and V) in which the reserve power of the heart must have been seriously limited, the comparatively good runs in the rebreathing test must have been made possible by efficient compensation through extracardiac mechanisms.

While the rebreathing test may offer a good indicator of the general fitness of an individual, the part the heart plays in any case in the adaptation to anoxemia is particularly difficult to evaluate because there occurs a coördinating of several mechanisms, some of which are known, doubtless others unknown. We have failed to

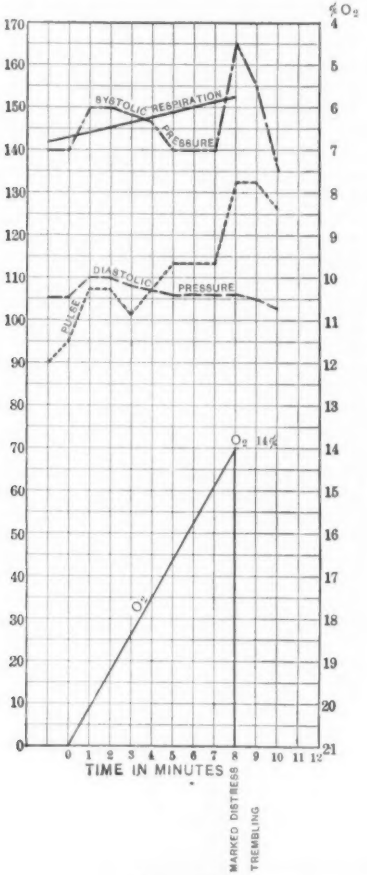

CHART VII

discover more than a moderate demand for increased cardiac function, in cases that we have tested, having been unable to demonstrate appreciable enlargement of the heart, either by observations on the position of the apex impulse, or by percussion of the area of cardiac dulness; nor have we observed the marked

engorgement of the vessels of the neck that almost invariably accompanies acute dilatation of the right side of the heart.

The variations in response to the anoxemia produced by means of the rebreathing apparatus, among cases with, at most, narrow margins of cardiac reserve, appear to justify the conclusion that the test does not furnish a trustworthy index of cardiac function.

BRONCHO-ESOPHAGEAL FISTULA AND TRACTION DIVERTICULUM.

By John B. Hawes, 2d, M.D.,
Boston, Mass.

The name "broncho-esophageal fistula" is self-explanatory, although the condition itself may be classified as one of the rarer lung complications. "Traction diverticulum" of the esophagus, differing only slightly in etiology and course from a simple broncho-esophageal fistula, is a still rarer complication, and one that finds scant mention in the literature. In the eighth edition of Osler's *Practice of Medicine* it is described as follows: "Traction diverticulum, situated in the anterior wall near the bifurcation of the trachea, results, as a rule, from extension of inflammation from lymph glands, with adhesion and subsequent cicatricial contraction by which the wall of the esophagus is drawn out. Diagnosis of this condition is now readily made with bismuth meal and roentgen ray." Osler mentions one case of an esophago-pleuro-cutaneous fistula in the right infraclavicular region which communicated with a cavity in the upper part of the pleura or lung. Osler and McCrae[1] describe a traction diverticulum as one caused by pressure from without; often it causes no symptoms. Tuberculosis of bronchial lymph nodes is a frequent cause. Little mention of either traction-diverticulum or broncho-esophageal fistula is to be found elsewhere in text-books on clinical medicine, while in works on pathology it is referred to briefly and as a rarity.

The diagnosis, as in one of my cases, is sometimes made by recognizing in the sputum particles of food eaten some time previously. Dr. W. H. Smith, of Boston, told me that he discovered one case purely by accident when on passing a stomach tube he met with an obstruction, and on withdrawing it found in the end of the tube several drops of pus which on examination was found to contain tubercle bacilli. The diagnosis of tuberculosis of the lungs and mediastinal glands was then confirmed by roentgen ray. Usually the diagnosis is impossible without a fluoroscopic examination. Dr. George W. Holmes, roentgenologist to the Massachusetts

[1] Modern Medicine, iii, 94.

General Hospital, has described to me an experience of his in regard to this: A patient suspected of having malignant disease of the gastro-intestinal tract was given the usual barium meal, the passage of which down the esophagus Dr. Holmes observed with the fluoroscope. To his surprise and considerably to his alarm, he saw a portion of the barium instead of going down into the stomach side-switched off into what were apparently cavities resulting from a cancerous involvement of glands around the lung root. The patient, however, suffered no unpleasant consequences in any way from thus having barium introduced into his lungs. It was his experience in this case in which the barium in the lung apparently did no harm that led me to risk this procedure in one of the cases herein described. One of these seen in consultation with Dr. Wyman Whittemore, and here presented with his kind permission, is an example of a simple broncho-esophageal fistula following an acute pulmonary infection, with resulting abscess of the lung; the other one of my own is a true traction diverticulum of the esophagus of some years' duration.

Case I.—G. T., aged thirty-seven years, a shoe-factory worker by trade, entered the west medical service of the Massachusetts General Hospital, November, 1919. One brother had died of tuberculosis. He gave a history of "pleurisy" at the age of eight years. His maximum weight was 148 pounds one year previous; his present weight was 130 pounds. Seven months ago he first noticed clubbing of his finger nails. His present illness began eleven months ago, when he was taken acutely sick with fever, pain in the right back and much cough and sputum. His physician told him that he had pneumonia. Five weeks after this a roentgen-ray examination was made which showed a consolidation of the right lung. A diagnosis of lung abscess was then made. Chest tap was negative. Soon after this he began to cough up as much as one pint daily of thick yellow sputum. Occasionally there was some clear blood. At the time of his admission he had constant pain in the right lower back, with considerable cough and sputum.

Physical examination showed dulness, with bronchial breathing, increased fremitus, crackling rales over the right upper one-third of the chest, with flatness, diminished voice and breath sounds and bronchophony at the right base behind. The heart was normal. He raised 20 to 24 ounces of sputum daily, which consisted of foul, bloody pus without tubercle bacilli. Wassermann test was negative. Roentgen ray showed a pathologic process within the right lung, with involvement of the pleura, appearing as "a dull, rounded area in the right lower chest." January 24, 1920, he was transferred to the surgical ward and operated on by Dr. Whittemore, who resected a rib and drained the abscess. February 1, 1920, it was first noticed that fluids which the patient drank partly came out through the

drainage tube in the wound in the back. This was conclusively demonstrated by giving him a drink of water containing methylene blue, which could be seen coming out through the tube. A bismuth roentgen ray was taken which showed clearly a sinus from the esophagus leading into the lungs. The report of this examination was was follows:

"February 12, 1920. Fluoroscope. A moderate portion of the barium mixture passed freely through the esophagus; a smaller portion was seen traversing the right lung field in an irregularly branching channel to the periphery of the chest. It appeared to leave the esophagus at a point opposite the upper portion of the aortic arch, but this area was not clearly seen on account of what appeared to be a superimposed density in the lung shadow.

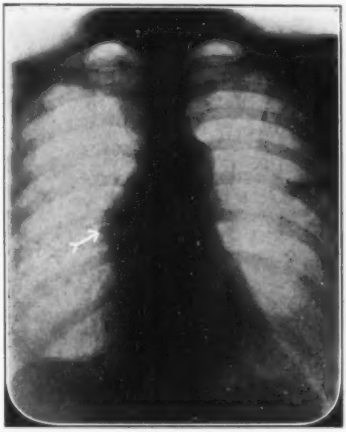

FIG. 1.—Arrow points to mass of glands at hilus of lung, probably the site of the traction diverticulum.

"The plate shows extensive dulness in the lower one-half of the right chest, as previously described. This dulness now rises to the level of the third interspace and is of a somewhat irregular density. Through this dulness can be faintly seen shadows of a small quantity of barium described in the fluoroscopic note. Diagnosis: Broncho-esophageal fistula."

The discharge from the opening in the back gradually lessened, the fistula healed up and the patient was discharged from the hospital April 5, 1920, apparently well.

Here then is a case of simple broncho-esophageal fistula following an acute pulmonary infection. The fistula healed spontaneously and the lung seemed to suffer no ill effects from the passage through it of barium or food, liquid or solid.

CASE II.—This patient was referred to me by Dr. W. H. Kenny, of Winchendon, Mass. S. H., a married woman, aged forty-two years, with two healthy children, aged seven and ten years respectively, first came to see me July 18, 1919. Her father died at seventy her mother at sixty-five years. She has three brothers and four sisters alive and well, but had lost one brother and one sister of tuberculosis. She stated that she had always been considered delicate, but except for frequent attacks of bronchitis had had no serious illness. Her maximum weight was 147 pounds at the present time. For the past fifteen or sixteen years she has had a slight hacking cough, with scanty sputum but no other symptoms. She stood childbirth splendidly, and her lungs were always declared to be sound.

In January, 1916, she came down with influenza while at the same time her children had whooping-cough. In her desire to look after them she got up too soon, had a relapse and for the first time had a copious pulmonary hemorrhage amounting to a "bowlful of blood." She was in bed three months, with marked weakness and loss of weight from 132 to 113 pounds. For a long period she had daily hemorrhages and was very seriously sick. In May, 1916, she gave up her home in Boston, where she was then residing, and went to live in the country, having been told definitely that she had consumption. Since August, 1917, although she has gained steadily in weight and strength, about once a month, practically always associated with her menstrual periods, she has had hemorrhages varying in amount from one or two teaspoonfuls to two or three ounces of clear blood. In the winter of 1917–18 she went to Florida and had three slight hemorrhages while there. At the time of this examination she had a good appetite, ate and slept well, and was without pain, fever or other symptoms except moderate shortness of breath. She was naturally in a very nervous condition on account of so frequent bleedings.

Physical examination when I first saw her in July, 1919, was practically negative except for the lungs. Here there was fairly definite evidence of an old, apparently tuberculous process in the right middle and upper lobes, with dulness in the region of the spine of the scapula, increased whispered voice and breath sounds and numerous dry rales. Roentgen-ray examination was as follows: "There is a well-rounded diaphragm of moderate excursion, not limited by adhesions. The heart shadow seems normal. There is considerable diffuse thickening at both lung roots in the peribronchial structures, with some old, calcified glands. There is moderate peribronchial infiltration about the finer bronchioles, particularly toward the right apex, and there is an area just in from the tip of the right scapula at the lung root in which the peribronchial structures are particularly thickened. There is some emphysema about this area and there is apparently what would seem to be a small cavity

here and also a thickened pleura between this upper and middle lobe of the lung. Aside from the calcified glands in the left lung root, with the very moderate peribronchial thickening upward, there is no evidence of any lesion on the left. We believe the hemorrhage could well come from this spot at the right lung root, which we believe to be probably tuberculous and fairly well localized."

As was to be expected I made a definite diagnosis of chronic, moderately advanced, pulmonary tuberculosis, despite the fact that my examinations and former examinations of the sputum had been negative.

December 4, 1919, I saw her again in consultation with Dr. Kenny at her home. She had done very well until five weeks ago, when

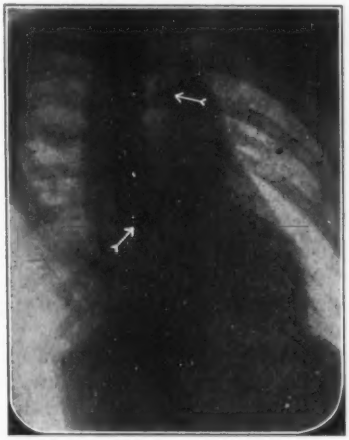

FIG. 2.—Lateral view of chest. Upper arrow points to esophagus partially filled with barium. Lower arrow points to shelf-like sinus on which part of the barium could be seen leaving the esophagus on its way to the lung.

she again started to raise blood in small amounts. About one week before this she had a slight attack of laryngitis, with a marked increase in the amount of sputum up to 6 or 7 ounces. This when I saw her had gradually decreased to normal. At this time her lungs were in apparently the same condition as before. The sputum consisted of pure pus full of pneumococci, but contained no tubercle bacilli, while her general condition was much improved. At this visit both the patient and her husband referred to the curious fact, which they were at a loss to explain, that particles of food eaten several hours previously were coughed up in the sputum. She was certain that these particles were coughed up and not vomited. She also noticed on swallowing an occasional sense of constriction or pressure to the left of the sternum near the fourth or fifth rib.

Dr. Kenny, her family physician, confirmed all these statements and wrote me as follows:

"For a number of years she has observed at times, twenty-four hours and more, after eating certain foods, such as oranges, that after coughing the sputum would contain particles of the above-mentioned food. She also has "coughed up" tablets or pills twelve hours after she had swallowed them, with merely the outside coating gone. I observed this morning particles of food mixed with purulent sputum, although she had taken no nourishment for three hours. You remember the pain she spoke of just to the left of the median line which would follow the act of swallowing food. Now I am wondering if it may be possible that she has a diverticulum of her esophagus and that it in some manner pressed on a bronchus and has caused ulceration of the same, finally breaking through it."

In January, 1920, this patient came to the Massachusetts General Hospital for further study. Here another roentgen ray was taken and likewise a fluoroscopic examination made while the patient was swallowing a barium mixture. Concerning this, Dr. George Holmes, roentgenologist to the hospital, reports as follows: "Fluoroscopic observation showed fairly good respiratory movements of the diaphragm on both sides; the costophrenic angles are clear. To the right of the spine, in the region of the lung root, there is a distinct area of increased density, in the center of which there are bright spots suggesting cavity formation. This process is somewhat nearer the back than the front of the chest and extends outward nearly to the mid-portion of lung. In the lateral view no mediastinal masses could be made out.

"Patient then swallowed some barium mixture. The bulk of this passed readily through the esophagus into the stomach, but there was a portion which seemed to rest in a shelf-like process in the esophagus opposite the lung root and near the point in which the area of increased density was noted in the lung. When the patient had taken a slightly greater amount of barium mixture it was seen to pass from this shelf into the bright areas previously noted, which had the appearance of cavities.

"A series of plates, including anteroposterior and lateral views, before and after taking the barium mixture, confirm the fluoroscopic observation, and show in the area described at the lung root a small, dense, round spot in the extreme outer portion of the invaded area. This spot is slightly further out in the lung field and rather more dense than the average calcified gland, and the possibility of its being a foreign body should be considered. The bright areas described in the fluoroscopic observation are even more noticeable in the plates and are probably due to cavity formation. The lung markings throughout both lungs are considerably thickened, but the thickening is most evident around the larger bronchi and in the lower parts of the chest. Such a thickening could be entirely due

to repeated infections. The apices and periphery of the lungs are clear. I can see no positive evidence of tuberculosis in the parenchyma of the lung. The process at the right lung root is probably chronic inflammatory. It may be or may not be of tuberculous origin. The examination with the barium mixture demonstrates a sinus communicating between the process in the lung and the esophagus."

Dr. Holmes and I both considered very carefully the question as to whether or not, in view of the fistula doubtless existing between the esophagus and the lung, the swallowing of barium could do any harm. We both felt confident, however, that if particles of food—orange, cascara tablets, etc.—that had been known to go down via the esophagus and came up by way of the trachea did no harm that a simple barium mixture would likely prove innocuous. That we were justified in this opinion has been shown by the subsequent course of events. Although previous to this time hemorrhages even under a most careful regimen were fairly frequent since leaving the hospital in January, 1920, when she was first given the barium meal, up to the present (June 1, 1920), she has had only one small hemorrhage, while her general condition has improved steadily.[2]

This case has been interesting in the extreme and the results so far at least very satisfactory to all concerned. Here was a woman in whom a definite diagnosis of pulmonary tuberculosis had been made by her family physician in 1916 and by myself in July, 1919, based on (1) signs in the lungs and (2) hemorrhages. Her husband gave up a flourishing law practice and went with his wife to live in the country. The patient, a very conscientious woman, had practically isolated herself from her children for fear of infecting them. As a result of careful study from my point of view it has been fairly well established:

1. Although the original infection of the mediastinal glands may have been one of tuberculosis this is not necessarily so nor definitely proved.

2. The patient is in no way a source of danger to those about her in view of repeated negative sputum examinations and her own high degree of intelligence.

3. It is no longer absolutely necessary for her to live an isolated life in the country, but, on the other hand, perfectly safe for her to reside within easy reach of Boston, where she and her husband's interests are located.

4. Finally although she has had and doubtless will have further hemorrhages, they will probably do her little or no harm, it having been shown that the process in her lungs is not a progressive one.

[2] Her general condition still remains good, but at intervals she still has severe hemorrhages, November, 1920.

From the physician's viewpoint this case has been an instructive one. It has more than ever confirmed me in my belief that the physician, who makes a definite diagnosis of pulmonary tuberculosis in the absence of a positive sputum, takes upon himself a grave responsibility. He should look at the case from every angle, from the patient's as well as from his own point of view, and should weigh carefully every bit of evidence pro and con before telling the patient that he is a consumptive.

It has likewise taught me that although the majority of pulmonary hemorrhages are due to tuberculosis, there are many of non-tuberculous origin, and that there are still more, that, although undoubtedly of a tuberculous nature, do not indicate active tuberculosis or that that patient needs anything more radical in the line of treatment than careful supervision and applied common sense.

Finally, I have been impressed with the fact that foreign bodies in the lung, in this instance, particles of food, cascara pills and barium do not have the disastrous effects usually supposed to be the case but that they may pass through the lung, as in Case I (broncho-esophageal fistula), to an opening on the outside, or pass from the esophagus to a cavity connected with the mediastinal glands and from here into the bronchi and out through the trachea, as in Case II (traction diverticulum), without apparently causing any disturbance or doing any harm.

CHRONIC NEPHRITIS: FROM THE POINT OF VIEW OF THE GENERAL PRACTITIONER. ITS DIAGNOSIS, PROGNOSIS AND TREATMENT.[1]

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When one examines the shelves of any complete medical library or merely goes over the titles on the subject of nephritis in any of the medical indexes and sees what an enormous number of volumes, monographs and articles were published on the subject in the last five to ten years, one must realize that in the time allotted to me we cannot possibly hope to adequately cover the ground. I have therefore decided to discuss the subject from the point of view as it affects the general practitioner and to raise only those problems which confront us daily in the management of these types of cases.

[1] Read before the Harlem Medical Society, October 13, 1920.

The Classification of Chronic Nephritis. Pathologists have taught us that we have a number of different types of chronic nephritis, namely:

1. Chronic parenchymatous nephritis with large white kidneys.
2. Chronic diffuse nephritis.
3. Chronic interstitial nephritis with small, contracted kidneys.
4. Amyloid kidneys, fatty kidneys, etc.

It is exceedingly interesting to note these differences in the anatomic structure of the diseased kidney as it appears on the autopsy table. But up to the present the most careful work, examination of blood, urine and kidney functional test have not yet enabled us to tell definitely whether in the living patient we deal with one type of kidney involvement or another. What we do know definitely is that we have a disturbance in the kidney function and that the different patients group themselves (1) according to the character of the physiologic disturbance and (2) according to the severity of the disturbance.

Besides, it is an open question today whether the anatomic differences that we observe on the autopsy table really represent different diseases which run their characteristic courses or whether they are different stages of progress in one and the same disease. The subject has recently been admirably discussed by Eli Moschcowitz. He brings evidence in favor of the latter view, and I feel convinced that the time is not far distant when that will be the accepted view of all clinicians and pathologists.

When I say that a patient has a phthalein output of 35 per cent. with a limited capacity for water and salt excretion while his nitrogen excretion is normal; or when I say that another patient has a capacity for normal phthalein output, excretes water and chlorides perfectly, but falls behind in his nitrogen excretion and shows retention of nitrogenous substances in the blood, we have given a decidedly clearer way of classifying our nephritic patients than if I said that the patient suffers from chronic diffuse nephritis or chronic interstitial nephritis. In the former way we can express the severity of the affection in definite mathematic figures and the progression or retrogression of the case can be followed, whereas by the latter classification we are left entirely in the dark. We therefore, from the practical point of view, must abandon the anatomic classification and take up the classification of our cases according to their disturbed physiologic function.

The Causes of Chronic Nephritis. It is in the nature of human inquisitiveness to look for a cause for every disturbance in the normal run of events. It is also natural for us to find something to blame it on. In regard to chronic nephritis, if we find the patient gives a history of scarlet fever, tonsillitis, malaria, pregnancy, exposure to cold, etc., we feel satisfied to put the blame on them. Since there are very few people who have not had one or more of the above

diseases, and since it is definitely known that scarlet fever, tonsillitis, malaria, etc., may be followed by acute nephritis, and since acute nephritis frequently is followed by chronic nephritis, the chain of evidence seems fairly well established that these infectious diseases are largely the causative agents of chronic nephritic involvement. In some cases in which we get a history of absolute well-being throughout the entire period of the patient's life, without any history of illness whatsoever, we put the blame on some "noxious poison" or some "product of metabolism" and let the matter go at that.

To my mind this does not at all seem a satisfactory explanation of the cause of nephritis. When we administer small doses of uranium nitrate to animals a severe form of nephritis is set up. It does not attack some and leave out others, but attacks every animal. The same is true for every nephrotoxic substance, be it cantharidin, lead, mercury, tartaric acid, oxalic acid, etc. They all attack the kidneys of every animal that receives the poison. When we see a large number of human individuals develop scarlet fever, some of most severe type, and come out with kidneys unaffected, whereas in others the mildest attack will be followed by nephritis, the same being true for tonsillitis, malaria, pregnancy, exposure to cold, etc., I cannot help but feel that these intoxications play but a secondary role, *i. e.*, merely an exciting role and that the primary seat of trouble lies in the kidney itself. We can readily conceive of organs in the human body at birth being of functional capacity below par. A great many combinations may go wrong during the period of embryonic development, especially during the period of differentiation, giving rise to single organs which may not be equal to the task thrown upon them in later life and which will break under the strain, giving rise to abnormal physiologic function, disease and finally abnormal pathology.[2]

I remember some years ago talking to Prof. Stockard, of Cornell University, on that very subject. Stockard, who is one of the foremost embryologists in this country, has devoted a great deal of his time to studying prenatal influences on development. He expressed his views at that time, saying that he believed that every person dies from the disease with which he is born. That during the period of differentiation the organ is marked out which is the weak link in the chain. Similar views are accepted now by all students of endocrinology in regard to endocrine disturbances, and one has to ponder only for a few minutes and go over the history of his cases to realize how true and how important that view is. The same view may be applied to cardiac and pancreatic conditions, diabetes, etc.

[2] I must say here that in my mind it is not at all a solved problem that altered structure precedes altered physiologic function. We must view the body as a chemical factory and we may have altered chemical conditions and altered physiologic results without being able to detect any changes in the cell structure by means of the microscope. For after all, while the microscopic examination of organs is a tremendous advance over the premicroscopic period, from the point of view of cell function it is a hopelessly crude method.

We recognize that we are all born with different degrees of mentality and intellectual capacity. We are also born of different stature and of different capacities for physical strength. Because of these differences we adjust ourselves on different planes in our social structure. These differences we can recognize early in life and do not attempt to force the prizefighter into a professorial chair nor the professor into the ring. We do not, however, look for differences in the functional capacity of the kidneys, lungs, heart, pituitary, thyroid, etc., as long as the individual feels well. Hence they go unrecognized. Any insult in the form of infection, or any strain, as pregnancy, may cause a break in the weak link.

My conclusion, therefore, in regard to the causes of nephritis is, that all the factors usually mentioned, as the etiologic factors, as infection, exposure, pregnancy, autointoxication, etc., are the precipitating causes, but underlying that the patient's predisposition plays the greater role.

If the individual goes on in life without any serious infection or intoxication he may stay well. As he progresses in life the weak organ is the first one to show signs of "old age" and begins to fall behind in its function.

The Physiology of the Kidney. Before we take up the discussion of the disturbances in kidney function that take place in chronic nephritis it will not be amiss to briefly review the physiology of the kidney.

Anatomically the kidneys are composed of a tremendous number of units. Each unit, in turn, is composed of five successive portions:

1. The glomerulus, surrounded by a capsule.
2. The proximal convoluted tubule.
3. The loop of Henle, consisting of a long descending and ascending loop.
4. The distal convoluted tubule.
5. The collecting tubule.

The glomeruli and the tubules are lined throughout their course with epithelial cells, but of different kinds of cells in different parts. In the glomeruli and loop of Henle we find flat endothelial cells, cells similar to those that we find in the walls of the capillaries, where there is the greatest opportunity for interchange of materials between tissue and blood. In the convoluted tubules we find epithelial cells of the type that we find in any secreting gland.

When we were students we were taught that it was the function of the kidneys to excrete urine, *i. e.*, water and all the soluble waste products of metabolism. This is essentially correct today. But now we must look at it from an entirely different angle—not from the point of view of the urine but from the point of view of the body and the blood.

We know that in the blood we have a fluid which is composed of a great many products of intermediary metabolism. We also

know that it is composed of proteins, sugar, lipoids, amino-acids, urea, uric acid, creatin, creatinine, purins, sodium, potassium, calcium, magnesium, iron, carbonates, sulphates, phosphates, chlorides, etc., the concentration of which is kept remarkably constant. We have also learned to know that the kidney exercises a remarkable selective power for its secretions so that these various substances are maintained at definite levels of concentration in the blood.

Take for example the excretion of chlorides. If an individual is on an absolutely salt-free diet the chloride in the blood will remain at a constant level and the kidney will refuse to excrete any of it, and we actually may find urines with merely traces of chlorides. On the other hand, if the person ingests a large amount of chlorides the moment absorption begins and its concentration in the blood tends to rise the kidneys begin to excrete the chlorides, so as to keep its concentration in the blood at a definite level.

The same is true for water, and it is perfectly remarkable with what promptness the kidneys respond to the ingestion of water.

The adjustment of the kidney with regard to glucose is really to be marvelled at. The blood contains normally from 0.08 to 0.12 per cent. sugar. None of it is excreted by the kidney, or if it is, as is claimed by Benedict, it is in such small traces that it can play no practical role. If, however, for one reason or another the glucose concentration reaches 0.13 to 0.15 or 0.18 per cent. the kidneys immediately begin to excrete it so as to lower its concentration in the blood.

Further, the animal body must be considered as a chemical factory in which acids and alkali are being formed all the time, but not to the same extent at different times. At one moment we may have a large production of acid, as during the period of high protein digestion; at the next moment we may have a large amount of alkali formed, as during the period of digestion of vegetables. The former state would tend to render the blood acid, the latter alkaline. The blood, however, under all conditions of health does not vary in its reaction at all: Why? Because the kidneys are adjusted with such sensitiveness to acid and alkali production that the moment one has a tendency to disturb the equilibrium, excretion of it begins immediately. Whether we are awake or asleep, active or inactive, on acid or alkaline diet, the blood will always be kept in what we have chosen to call a normal state of purity. It is the function of the kidneys to keep it thus.

Do you know that it takes a certain amount of salt to keep the globulins of the blood in solution, and what might happen if the globulins were to precipitate out in the blood for lack of that amount of salt? The red blood corpuscles are cells that require certain definite osmotic conditions in the blood for their proper functioning and to prevent them from either shrinking or laking. These conditions can only be maintained by a certain definite water to salt relationship.

The osmotic pressure of the blood is measured by determining the depression of the freezing-point and the extreme variations under all conditions of normal life are only from −0.56° to −0.58° C. It is the function of the kidneys to regulate these relationships and to permit no disturbance whatsoever.

From all this we see that while it is the function of the kidney to excrete urine, of far greater importance is its function in maintaining the proper equilibria in the blood. And from the point of view of understanding what happens in the nephritic individual, this is of the utmost importance.

Until now we have discussed the functions of the kidneys *en masse*, we shall now devote a few moments to a review of the mechanism of urinary secretion.

As was said above, the kidneys are composed of functional units which are made up of glomeruli, distal and convoluted tubules, loops of Henle and collecting tubules. The glomeruli and loops of Henle are lined with flat endothelial cells, whereas the convoluted tubules have epithelial cells of the type that we find in all secreting glands. On the basis of the peculiar funnel-like structure of the glomeruli it was early assumed that the urine was filtered through it by purely physical means. All the experiments today tend to support this view, and it is definitely established that water and salt are excreted mostly through the glomeruli, while the tubules, especially the convoluted portions, excrete most of the nitrogenous constituents like urea, uric acid, creatin and creatinin. The urine as it passes out of the glomeruli is of very low concentration, similar to that of the blood. In its passage through the various tubules water is reabsorbed, so that by the time it reaches the pelvis of the kidney the urine becomes vastly more concentrated than the blood.

Pathologic Physiology in Nephritis. On the basis of the above physiologic considerations we may readily see that any disturbance in the glomerular function will be followed by a disturbance in the water and salt elimination, which means an accumulation of water in the tissues, with edema and general anasarca, depending upon the severity of the case. A patient like this may have no trouble eliminating the products of protein metabolism like urea, uric acid and creatinine.

On the other hand, disturbances in the tubular portion of the kidney will cause interference with the elimination of urea, uric acid and creatinine, while water and salts may be secreted perfectly.

As a matter of fact all the cases of nephritis that we come across belong to one or the other group in their early stages. In their later stages the whole system is likely to break down and there may be interference with both water, salt and nitrogenous elimination.

The tubular type is by far the more common. Of 230 cases of nephritis that I have had the opportunity of studying in the past few years only nine were of the glomerular type. Why the tubular

part of the kidney should be so much more vulnerable is a difficult matter to answer. Perhaps it might be explained on the basis that the tubular cells have more positive work to do in secreting solid substances, like urea, uric acid and creatinine, than do the glomerular cells in passing water and salts. And it is a matter of common knowledge that the least soluble of the three—uric acid—is the first one to fall behind in kidney decompensation and the first one to be found retained in the blood. The tubular cells may become fatigued earlier in life and break under the strain.

The Clinical History of Nephritis. To properly appreciate the development of the clinical history we must bear in mind a few facts:

1. That the amount of kidney tissue that is possessed by any normal individual is much greater than his physiologic requirements, *i. e.*, as far as excreting cells are concerned, we have a large factor of safety. It has been demonstrated that we may remove one kidney completely and a good portion of the second one, and there will be left enough kidney tissue to carry on the normal functions.

2. There are no subjective symptoms and there may be no objective symptoms for a long time after disturbance in the kidney function has set in.

3. That all the symptoms of nephritis are symptoms of deficiency in kidney function.

With these three facts in mind we can readily see why the disease sets in so insidiously, and a patient may go on for years and years developing chronic nephritis without its being detected. It is because of this point that the education of the public to subject themselves to a systematic medical examination at regular intervals becomes of great value. A large proportion of all the nephritic cases that I have seen were first recognized while applying for life or health insurance or by organizations like the Life Extension Institute.

The early history of chronic nephritis is entirely obscure. Symptoms develop only later, and these may vary in different individuals. The earliest cases that I have come across are those that have come to me complaining of having been refused life insurance. These people feel perfectly well and are inclined to discredit the value of the insurance examination. On careful examination I find these patients may have a slight elevation of blood-pressure, 140 to 180 systolic and 75 to 80 diastolic. There may or may not be small traces of albumin and a few casts in the urine. Quantitatively the urinary output is normal, the nitrogen and chloride elimination is perfect, while all the functional tests of the kidney show normal activity. These individuals have absolutely no subjective symptoms whatsoever and the objective symptoms may not always be present. For future reference, we shall designate these cases as belonging to Group A.

The second group of cases are those that have some subjective

symptoms. They come complaining of a tired feeling, especially in the afternoons. They do not feel as ambitious as they used to. They may have frequent attacks of headaches, with momentary dizziness; they may have slight shortness of breath and palpitation of the heart on exertion. Examination shows essentially the same findings as in the case of Group A, except for the fact that the blood-pressure may be higher. We may find here cases with a blood-pressure of 200 and there may be decided left ventricular hypertrophy. The urinary examination may show the presence of fairly large amounts of albumin and a few casts; the great majority have only a small trace or none at all. All the functional tests are normal; the blood examination is normal. We shall call these cases Group B.

To the next set of cases, Group C, belong the vast majority of my cases. Most of their symptoms are referable to the cardiovascular system. They come complaining of frequent headaches, dizziness, palpitation of the heart and shortness of breath on the slightest exertion, dark spots in front of the eyes, insomnia, anorexia, edema of the legs, puffiness under the eyes, ringing in the ears, pain in the precordium, etc. On examination these patients are found to have systolic blood-pressure anywhere from 180 to 280 and diastolic from 80 to 150. The great majority of them show a good myocardium, with hypertrophied left ventricle, while a number of others show decided evidence of failing myocardium, the symptoms depending, of course, upon the degree of cardiac insufficiency.

To the last, Group D, belong all those cases of nephritis which show unmistakable signs of kidney deficiency or decompensation. Whether it be poor water and salt elimination with edema, poor phthalein elimination or retention of nitrogenous products in the blood. They show signs of intoxication of varying severity and are mostly bedridden. As a group they give the impression of being very sick. They may have gastric disturbances like anorexia and vomiting. In the later stages they may develop a peculiar uriniferous odor. As a rule they have all kinds of complications, especially in the cardiovascular system. There may be nervous and mental symptoms, varying in degree from severe headaches, insomnia, neuralgic pain, retinitis, diplopia, temporary blindness, etc., to full-fledged attacks of irrationality, convulsions and coma. Examination of the urine will show the presence of large amounts of albumin and casts. The quantity of urinary output may vary and may depend largely upon the degree of cardiac complication.

We may therefore, in view of the above, recognize four degrees of severity in the course of chronic nephritis.

Group A. In which the patient has no subjective symptoms whatsoever, and not very marked nor permanent objective symptoms.

Group B. In which the patient has slight subjective symptoms, usually referable to cardiovascular disturbances, and the objective symptoms more marked and more permanent.

Group C. In which the patient has fairly severe subjective symptoms and the objective findings of nephritis are quite marked. Functional tests still show normal elimination of known products of metabolism.

Group D. In which the patient shows the first unmistakable signs of kidney functional break-down or decompensation, with severe cardiovascular or nervous symptoms and the beginning of uremic symptoms.

Diagnosis of Chronic Nephritis. The diagnosis of chronic nephritis in the later stages or when albumin or casts are present is a very simple matter. The difficulty, however, is presented by those groups of cases which have negative urinary findings, *i. e.*, no albumin and no casts, and still show a great many of the symptoms that we find in chronic nephritis, namely, high blood-pressure, cardiac hypertrophy, arteriosclerosis, retinitis, etc. A certain school of clinicians are inclined not to connect these cases with nephritis but to put them in a class by themselves as cases of essential hypertension.

We all know that we may have severe cases of chronic nephritis, with a tremendous amount of interference in kidney function and only traces of albumin. We also know that we find large amounts of albumin in urines of individuals who never have more than a mild type of kidney interference. In other words the amount of albumin in the urine, and for that matter, also, the number of casts in the urine, are in no way criteria of the severity of the case. If the slightest trace of albumin is detectable in any case of hypertension, even the greatest enthusiast of the essential hypertension idea would diagnose it as nephritis. Are we justified, then, in the absence of those traces of albumin, in disconnecting cases of hypertension from chronic nephritis, especially so, when we know it as a fact, that every case of hypertension, if it does not suffer a cardiac break-down or cerebral hemorrhage, will ultimately show unmistakable signs of severe nephritis, and when these do develop, the course to the final break and uremia is a very short one indeed.

Chronic nephritis, high blood-pressure and hypertrophied heart cannot be separated from one another. They are a series of links in a closed chain, forming a complete circle, and at the present stage of our knowledge we cannot say definitely whether the chain begins here and ends there. There are just as many arguments in favor of its beginning there and ending here. The question whether chronic nephritis is the cause of high blood-pressure or whether high blood-pressure is the cause of nephritis should be left open, and from the point of view of protective therapy, I personally am inclined to consider every case of hypertension as a potential case of chronic nephritis, just as I am inclined to consider every case of nephritis a potential case of uremia.

We have made enormous progress in the study of the chemistry

of the blood and in the study of nephritis from the point of view of the blood. But can anyone say that we have completely exhausted the field and that we know every substance that is present in the blood which should have been excreted by the kidneys? We cannot. There may be any number of substances retained by the kidneys which will account for a rise in the blood-pressure.

Take, for example, gout. Who would have believed, fifty years ago, that the uric acid accumulation in the blood was due to the failure or difficulty on the part of the kidneys to excrete it? But this is the case, and from the modern point of view it may be considered a specific form of nephritis which in the great majority of cases develops ultimately into ordinary nephritis.

That we find peculiarities in different individuals with apparently normal kidneys in regard to their power to excrete different substances we know from different sources. We know, for example, that some kidneys will excrete sugar when the blood sugar concentration is only 0.10 per cent., while others will not excrete it even when the concentration reaches 0.26 per cent. The latter is certainly "nephritic" as far as sugar is concerned. Idiosyncrasies to drugs like bromides, iodides, arsenic, etc., may also be explained on the basis of specific failure to eliminate those substances.

On the basis of all the above, I would therefore suggest that chronic nephritis should not be diagnosed alone on the basis of the presence of albumin and casts—these are too unreliable—but on the basis of the general clinical findings. And it is safer, as far as therapy is concerned, to diagnose a case as of potential chronic nephritis than of essential hypertension.

Prognosis of Chronic Nephritis. The ability to prognosticate the outcome of any disease is a skill which takes years of experience to acquire. It is not one which can be transmitted from master to pupil. It is not like science, that can be learned, but more like art, acquired from within by intuition. A good prognosticator is one who has a faculty for correct judgment, a thorough realization of the patient's condition and the ability to detect in advance possible complications that may set in and their effects upon the patient, plus a vast experience with a large number of cases of a similar nature.

Prognosticating practically means prophesying, and one knows what the world thinks of prophecies that prove false. The patient, and particularly his family and friends, are very much concerned with the course of any disease and expect the physician to tell them the outcome. One's wisdom must receive a terrible jolt after pronouncing a bad prognosis and declaring a patient hopeless and sure to die, to meet him months or years later and be reassured of the "bad" prognosis. It is equally unpleasant to hear of the patient's death after having made optimistic prognoses.

Anything, therefore, which tends to transfer prognosis from the

plane of art, guesswork or speculation to that of science, will mean a tremendous step forward. Fortunately for us in the field of nephritis a step like this has been made during the past ten years, and we may add here, with not a little pride, that most of the work was developed in our own country.

The course of the disease in nephritis depends entirely upon the functional capacity of the kidneys, and by determining that we can foretell with a fair degree of accuracy, what the result will be. Of course, we must ever be mindful of the fact that with chronic nephritis we do not deal with kidneys alone but with a myocardium which may suffer insufficiency and with cerebral arteries which may rupture—all of which may upset our conclusions and direct the patient's course into different channels.

The Functional Tests in Nephritis. There are three functional tests that we employ today, each of which has its special advantages.

1. In the first test we administer certain substances to the patient and study the speed with which it is excreted by the kidneys in the urine. Most of these substances are foreign to the body. These are potassium iodide, lactose and phenolsulphonephthalein. Of these the last one is the easiest to carry out and gives a fairly reliable indication of the condition of the kidney.

In the morning, before breakfast, the patient is asked to empty his bladder. He is then given 400 c.c. of water to drink to ensure free diuresis; 1 c.c. of phenolsulphonephthalein solution, containing 0.006 gram of the drug, is then injected intramuscularly in the lumbar region and the time noted. Exactly one hour after the injection the patient is asked to void urine in a cylinder and is given another 400 c.c. of water to drink. At the end of the second hour he is asked to empty his bladder again. To each cylinder of urine a small amount of concentrated sodium hydroxide solution is now added, which brings out the purplish-red phthalein color and the volume of each specimen is brought up by adding water to 1000 c.c. The color of a small sample of this is now matched up with a standard solution and the percentage of phthalein excreted calculated.

A kidney that has sufficient functioning cells to carry on the required excretion of the products of metabolism will excrete not less than 35 per cent. of the phthalein during the first hour and about 20 to 25 per cent. during the second hour, a total of 55 to 60 per cent.

Cases belonging to Groups A, B, and C give normal phthalein figures. Although in Group C we may meet with cases of advanced nephritis, still we will get normal phthalein elimination because there are enough functioning cells left to carry on the work. The prognosis for the immediate future, as far as the kidney is concerned, is good. Of course before making this prognosis one must be circumspect of the cardiovascular condition of the patient. If the blood-pressure is moderately high, say about 200 systolic and about

90 to 110 diastolic, with a heart that is not irritable and only moderately hypertrophied, the prognosis is good and may continue to be good for quite a long time. If the blood-pressure is around 250 or over and the diastolic pressure is around 130 to 150 the outlook is not so good. For some reason or other high diastolic pressure invariably presages myocardial trouble. Frequent attacks of palpitation of the heart in this stage is another unfavorable sign in determining the prognosis.

When we find only 45 to 40 per cent. of phthalein elimination in the two hours it means that the kidneys are beginning to fall behind in their work, which is a very serious matter. It means the patient's entrance into the Stage D of the disease. We must therefore be very careful that no extraneous influence has affected our results. It sometimes happens in men with enlarged prostates and in women with prolapse of the uterus and cystoceles that not all of the urine secreted by the kidneys in a given time is actually voided. During the two hours more phthalein will be excreted by the kidneys than is delivered by the patient into the cylinder, because a considerable portion is retained in the bladder. It is therefore important to repeat the test when low results are obtained, catheterizing the patient at the end of the second hour and washing the bladder out with distilled water.

If on repeated tests the phthalein output is low the prognosis is very serious. While a patient may have nephritis throughout practically his entire life, and I have seen cases of nephritic histories of more than thirty years' duration, a patient cannot live very long with a decompensated kidney. Once the kideny begins to fall behind matters soon get beyond one's control. Once the patient has broken through into Stage D the phthalein output will keep sinking until a condition is reached in which there is no output at all. Of course you must realize that the downhill course is not in a straight line. There may be temporary improvements, because so much of the kidney function at this stage is dependent upon ups and downs in the circulatory apparatus. But on the whole the outlook is very grave both for the immediate and ultimate future.

In the phthalein test we find a ready and quick method of orienting ourselves as to the patient's functioning capacity. It requires simple apparatus, little expense and above all very little discomfort to the patient.

The second functional test is made by a quantitative study of the urinary output. This was first suggested by Schlayer and Hedinger and developed in great detail by Mosenthal and his coworkers. For the past few years I have worked on this method and succeeded in modifying it.

The test as it is carried out is based on the following consideration: If we collect the urine of any normal individual for twenty-four hours in two twelve-hour portions, starting the first twelve hours

at 8 A.M. and closing it at 8 P.M., and the second 12-hour period from 8 P.M. to 8 A.M. the following day, taking care the individual has his principal meal in the daytime, supper at 5 P.M. and does not eat or drink after that until the following morning, we find that the relationship of day excretion to night excretion for nitrogen is roughly 3 to 2 and for chlorides it is 3 to 1 or 4 to 1. The nocturnal water output will be, as in Mosenthal's results, less than 400 c.c. The reason for this is the following: A normal individual ingests most of his food during the twelve hours of the day. As quickly as the products of digestion become absorbed and metabolized the products of metabolism, like urea, uric acid, chlorides, etc., enter the blood stream. As their concentration in the blood increases the kidneys begin to excrete them in the urine. Normal kidneys respond so promptly that comparatively little is left for the night excretion. Therefore do we have a comparatively low nocturnal water output, and the ratio of day to night elimination of solids is as given above.

If, however, the kidneys do not respond so promptly and begin to fall behind in their work some of the material which in a normal individual would be excreted during the day is eliminated during the night, and the proportion of day to night chloride and nitrogen excretion will tend to approach each other. There will also be nocturnal polyuria, because with the excretion of more solid materials during the night there is also excreted a larger amount of fluid.

By morning all the nitrogenous products from the blood are excreted, and if we examine the blood then it will be found normal in its nitrogen products concentration.

We can thus see that by studying the shifting of the day to night ratios in the nitrogen excretion we can detect an approaching kidney insufficiency long before the blood figures change.

This method has advantages over the phthalein test because in addition to giving information of the degree of kidney function it also gives us an idea of the special interference—whether it is water, chlorides or nitrogenous material that is excreted with difficulty. And from the therapeutic point of view, this is of much greater value.

The third test for kidney function consists of examining the blood for products of metabolism, which are normally found in very small quantities, and which are found very much increased in cases of renal insufficiency. These are urea, uric acid and creatinin.

The blood of a normal individual in the morning before breakfast contains not more than 3 mg. of uric acid, 20 mg. of urea nitrogen and 2 mg. of creatinin per 100 c.c. of blood. In renal insufficiency when the kidney first begins to fall behind in its work, the uric acid is retained first, doubtless due to its insolubility, which gives the kidney the greatest difficulty in excreting it. The figures mentioned above (3 mg.) are the upper normal, and any figure above that is already of grave diagnostic importance. Next to the uric acid the

urea nitrogen begins to climb and may reach to 150 and more milligrams per 100 c.c. of blood. Lastly, the creatinin begins to rise, and when we find creatinin concentration go up to 5 mg. per 100 c.c. of blood the case is absolutely hopeless and death from uremia is imminent. I know of only one case that lived with high creatinin in the blood for some time. All others succumbed within a very short time.

I should like to say here, in passing, that the results of these methods are of the utmost importance. The chemical procedure has been worked out carefully, and it takes careful and skilled chemists to make these determinations, so that they will be of value. When entrusted to technicians who know only the motions and do not understand what they are doing, apparently conflicting results are frequently obtained.

The Treatment of Chronic Nephritis. The treatment of a disease like chronic nephritis, in which we can find no one definite cause to remove and for which we have no specific remedy, offers exceedingly great difficulties. Our treatment must be directed along three channels: (1) To ameliorate the patient's symptoms and to make him comfortable; (2) to attempt to check the progress of the disease; (3) to prolong the patient's life.

You will recall that in the early part of our discussion I described four stages of severity in the clinical course of chronic nephritis. In Stage A I placed all those cases that have no subjective symptoms whatsoever but have some objective symptoms which are not very marked nor permanent.

The cases I have seen belonging to this stage are not very numerous, about 20 in all. Those who are engaged in the general practice of medicine have the opportunity of discovering them. I use the word "discover," because they come to you for other reasons, not being aware of the existing renal involvement. A great deal can be done for these people at this stage which cannot be done later.

A great deal of tact must be used in announcing to a perfectly well-feeling young man or woman, at the height of their careers, that they have some renal involvement or high blood-pressure. It is a terrific shock to the great majority of the patients. Most people immediately associate it with the worst complications and early death; neither of which is correct. I consider it a terrible crime to tell a patient with high blood-pressure that the bloodvessels in his brain are likely to burst any moment or that he is sure to die in a few months or years. Patients with chronic nephritis and high blood-pressure have been known to live to a good old age. I have one patient, a woman past seventy years, who was treated by the elder Dr. Janeway for some twenty years for her blood-pressure and kidneys. Then she was a patient of Theodore Janeway's, and I have had her under my care for the past five years. Her blood-pressure is never below 220 and very frequently around 280. She

takes good care of herself and has lived a long and useful life in spite of her physical limitations.

The early recognition of these conditions is of the greatest importance—not because these patients require early treatment. No. They require no treatment at all, and the more we let them alone the better. But because it is of great importance that they learn to rearrange their mode of living. To be moderate in all their habits; not to overeat; not to overdrink; not to overwork; not to subject themselves to unnecessary excitement; not to engage in violent exercise, etc. It will not do for a young man, aged thirty years, with a blood-pressure of 160 to 170, to be engaged in a work which will keep him running up and down stairs. Nor will it do to have a man in a similar condition, with decided evidence of renal lesion, engaged in work in which he is continually exposed to drafts and extreme changes of temperature. It is our duty to explain to those people, and to make them realize, that while they have a physical limitation, with care they can live out their lives, and that it is in their own interests to quickly adjust themselves to their condition. It is indeed a hardship for a father of a family to have to throw up his work and seek a more sedentary occupation, but this is the time to do it and not when it is too late.

The patient's gainful occupation and his physical condition are very intimately related, and we clinicians must enter into that phase of the patient's life. We must take it upon ourselves to convince the patient of the advisability of making the change if we feel that his work is injurious to his health and we feel assured that the change will benefit him.

I consider the rearrangement of a patient's social status to his physical condition the greatest step toward preserving his health and prolonging his life. Next comes the regulation of his habits of eating, drinking and smoking. We must also inquire into the patient's mode of spending his leisure time and into the number of hours he spends in sleep. Restful hours and plenty of sleep add a great deal to the patient's well-being.

It is also important at this stage to look after the general hygienic condition of the patient, to teach him to look after the regulation of his bowels and the condition of his teeth and tonsils. When the patient's functional capacity of the kidney is good there is no necessity for restricting the diet too much. He can have an amount of protein corresponding to about 10 to 12 grams of nitrogen per day. I usually advise the elimination of all meat soups and excessive salt from the diet. There is a feeling in the profession that eggs are harmful to nephritic patients. This is not so. Eggs for the nephritic are as healthful a food as for any other patient.

With the exception of a possible dose of bromides, to help tide over the nervousness caused by the disturbance in the patient's life, it is not advisable to use any medication at this stage.

I have seen patients at this stage fed on lithia tablets, nephritic pills, nitrites, diuretics, alkali and what not. We should realize what these patients need at this stage. The circulation is good, the kidney function is good—why disturb them? Why give them alkali to excrete and thus throw extra burdens on the kidneys? Why give them diuretics and drive an already tired organ? The more the patient is let alone the better.

What was said for patients of Stage A is equally true for patients of Stage B. We are not dealing with people that are sick but with people who suffer a physical handicap. Our chief duty now lies in preventing the patient from doing things which might hasten a breakdown. If he develops slight edema of the ankles, or if the blood-pressure runs up too high, it may be advisable to place him in bed for a week or two. It is remarkable what a tremendous effect this has on the patient. I have seen cases with blood-pressure of 220 and 240 come down to 160 and 180 after spending only one week in bed. The use of nitrites in these cases is of absolutely no use, except if the patient has anginal attacks. In that case I give him 1 grain of sodium nitrite or $\frac{1}{50}$ grain of nitroglycerin. The use of benzyl-benzoate, recently advised by Macht is of no use whatsoever.

Before prescribing a drug to a patient with nephritis it is advisable to know what one wants to accomplish, what symptom or group of symptoms one wishes to eliminate and to watch for the effect. If we do get a response, stop the drug immediately. If we do not get any improvement, continuing the drug will not help but may introduce serious complications. I remember 2 cases, 1 in private practice and 1 in the hospital, that I was called in to see. Both patients had high blood-pressure, with albuminuria and casts. The history of both was that for the past few days they had been getting more and more stuporous, until finally they could hardly be aroused. The diagnosis of uremia was made in both cases. From both the examination and the general history one could hardly come to any other conclusion, but on examining the blood we found its chemical composition normal, save for a slight increase in the uric acid. As we shall see later, patients with uremia never have normal urea nitrogen. The diagnosis of uremia had therefore to be abandoned. It was then brought to light that both patients had been taking chloral hydrate for several weeks. I felt convinced that the chloral hydrate was responsible for the complications. Several days' abstinence from the drug cleared up both cases. Both patients are alive today.

We must ever be mindful of the fact that most drugs have to be excreted from the body and that it is done very largely by the kidneys. Therefore it is important when drugs have to be used to select only those that cannot possibly aggravate matters and introduce complications.

There are a great many patients who believe that the "albuminuria" or the "high blood-pressure" constitutes their illness, and they expect the physician to "cure" them of it. A fifteen minutes' talk, in which the whole matter is explained to the patient and brought within his mental grasp, will save a lot of trouble in the end.

Success in the treatment of such a condition depends not upon drugs or medicine but upon teaching the patient to recognize his limitations, to save himself every bit of unnecessary exertion, to readjust his activities, to regulate and moderate his diet, to spend as much of his time at rest as possible. In other words, to teach the patient to live within his physiologic means.

Patients who are classified as belonging to Group C are mostly ambulatory, still engaged in gainful occupations, but who begin to find it a great burden to get through the day's work. They suffer primarily from symptoms affecting the cardiovascular and nervous systems. As far as the kidney function is concerned there is still perfect elimination of all the known products of metabolism, though in the later stages there may begin evidences of delayed excretion.

The treatment is entirely symptomatic. Headaches, dizziness, palpitation of the heart and shortness of breath form the chief complaints of most of the patients in this stage. Seldom will these symptoms be manifest in patients who have a blood-pressure of less than 220 or 240. When this does occur the patient's myocardium is usually at fault. Obesity may also frequently be responsible for it when accompanied by a not too strong myocardium.

The best and most efficient remedy, and one which seldom fails, is one or two week's vacation in bed, with a dose of bromides, 15 grains three times a day. During this period I restrict the diet to a low protein, low salt and low purins, *i. e.*, cut out meat soups, tea and coffee. In addition, I also restrict the absolute amount of food. If the headaches and dizziness are very severe the use of cinchophen tablets, in 7-grain doses, two or three times a day, is frequently of great benefit. Tolysin in 5-grain doses may also be used. The latter has the advantage of being tasteless and does not tend to produce gastric distress. Phlebotomy and withdrawal of 300 to 500 c.c. of blood is frequently followed by relief. I have had several patients who suffered such intense headaches that nothing but morphin could relieve them. The performing of a lumbar puncture and withdrawal of some of the spinal fluid plus a venesection brought them considerable relief, and they were able to get along without drugs for a long time afterward.

Staying in bed, free from excitement and business worries, has positively the most soothing effect on a patient. He gets a new lease of life and feels better for months afterward.

I usually prescribe the following diet during this period of rest:

Breakfast:
- Stewed fruit.
- Cereal and milk.
- 1 slice of bread and butter.
- ½ cup of milk, hot water and sugar.

Lunch:
- Cream of celery, cauliflower or tomato soup.
- Rice cakes, potato cakes or pea croquettes.
- Green vegetables.
- Salad: lettuce, tomatoes, olives, with olive oil.
- 1 slice of bread and butter.
- ½ cup of hot water and milk.
- Dessert: puddings, custard or ice-cream.

Supper:
- The same as breakfast.

If hungry between meals, half a glass of zoolac or fermilac.

When the patient returns to business it is not necessary to have the diet as strict as this. As long as there is no sign of retention I allow meat, poultry and eggs to such an extent that the urinary nitrogen does not exceed 10 to 12 grams per day. This is a comfortable diet and allows plenty of variety.

Breakfast:
- Fruit of any kind.
- Cereal with milk or cream.
- Bread and butter.
- Milk, Kaffee Hag or Postum.

Lunch:
- 1 or 2 eggs.
- Fruit salad.
- Bread, butter and milk.
- Dessert: custard, puddings or ice-cream.

Dinner:
- Milk soups.
- Fish or meat—1 or 2 ounces.
- Vegetables of all kinds.
- Salads.
- Bread and butter and milk.
- Desserts.

The patient is advised to use salt and pepper and other condiments in great moderation. The use of alcohol in small doses, in dilute form at infrequent intervals, is not to be objected to if it agrees with the patient.

Variety in diet is very important, for if they do get the same thing they will soon tire.

Edema of the legs is a very frequent complaint at this stage. It

usually comes on in the afternoon and passes away overnight. I know of nothing that works so surely for its eradication as rest in bed.

It is well to warn patients in this condition of some of the complications that may beset them and which may prove to be of great danger to them: (1) Upset stomach, with vomiting; (2) constipation and the habit of straining at stool; (3) catching cold, with developing attacks of coughing. Every one of these is preventable if the patient will only take care.

Cardiac complications are very common at this stage and very frequently the patient will suffer from various degrees of cardiac dilatation, with relative mitral and aortic regurgitations. This is very serious and invariably affects the course of the nephritis very adversely. The kidney function depends entirely upon a perfect and proper supply of blood. A perfectly normal kidney's function may be arrested if the blood supply is interfered with. Think of what must happen to the struggling cells of a degenerated kidney when the blood supply becomes irregular and incomplete! We frequently find marked oliguria develop, and if the patient should happen to be drowsy, or unusually irritable, irrational or perhaps have some convulsive seizure, the diagnosis of uremia is frequently made. I take this opportunity of calling your attention to one thing, namely, that we must reserve the term uremia specifically for those cases in which we have renal insufficiency, with retention of the products of metabolism in the blood. Uremia should not be diagnosed on the basis of the clinical symptoms but on the basis of the blood findings. Dozens of times have I seen uremia diagnosed on the basis of clinical symptoms without corroboration by blood findings and events proved later that uremia was not the cause of the complex.

Oliguria and nervous symptoms in nephritis, with cardiac decompensation, do not always mean uremia, unless it is associated with a marked increase in the uric acid, urea and creatinin concentration of the blood. If this is not the case the heart is the primary offender and the patient should be treated vigorously with digitalis and the other known cardiac stimulants. In no case of chronic nephritis have I seen any benefit gained by the use of diuretics, like diuretin, but when oliguria is due to cardiac decompensation the effect of diuretin is simply marvellous. The administration of 20 grains of that drug two or three times per day may convert a 200 c.c. urinary output per twenty-four hours into an output of 2000 c.c.

A word about the acidity of urine and its concentration in cases of cardiac insufficiency: I have seen physicians worry a great deal about it and frequently prescribe alkali, sodium bicarbonate, in rather large doses, which frequently upsets the stomach and brings on attacks of vomiting and also diarrhea, with gas distention of the

intestines, etc. The truth of the matter is that the acid in the urine does no harm to the patient. The blood alkalinity, measured by the carbon dioxide capacity, is usually normal in those cardiac cases. As far as the concentration is concerned it is bound to be high, for in those 200 c.c. the patient will excrete practically all of the nitrogenous matter. Water and salts are the only substances that are held back in cardiac decompensation, that is why those cases have severe edema and general anasarca but no uremia.

If alkali must be given it is wise to give it in small doses—5 grains, or at most 10 grains, at a time.

We shall now take up the treatment of the last stage of nephritis, namely, Stage D. Unfortunately this is a thankless task. We are dealing with a group of people who no longer possess enough functioning cells in their kidneys to excrete the normal products of metabolism. The result is that these products tend to accumulate in the blood. The human individual metabolizes three kinds of foodstuffs, carbohydrates, fats and proteins in addition to salts and water. The products of carbohydrates and fats are carbon dioxide and water. The former is excreted by the lungs, the latter by the kidneys. The products of protein metabolism are urea, uric acid, creatinin, amino-acids and a number of other substances, which can be excreted only by the kidneys. A normal individual must receive a certain amount of protein to maintain himself in protein equilibrium. The patient in Stage D cannot receive that amount of protein. He must be kept on a protein level commensurate with his ability to excrete nitrogen, and as the latter sinks the intake must be diminished. As far as nutrition is concerned, everything must be subordinated to the patient's renal capacity or else collapse is inevitable.

Some of these patients have very violent symptoms, others are more fortunate. In either case the outlook is very grave. The treatment depends largely upon the symptoms and should also be directed toward helping the body rid itself of the retained products and preventing the accumulation of new products.

If the patient has difficulty with water and salt elimination edema will be the most prominent feature of the symptoms. Salt-free diet and restricted water intake are absolutely essential. Everything must be cooked or baked without salt. If the nitrogenous excretion is good I allow them sufficient protein. On such a diet the edema will gradually improve. The use of diuretics is absolutely contra-indicated. We may get an increase in the water output for a day or so, and after that it is worse than before. Digitalis may be of help, probably because it spurs up the heart, and should be used, cautiously. Frequent purgation, by means of salts of magnesia, is of great value. Diaphoresis may also be of service if not overdone. Hot packs, hot air baths or electric baths are good remedies. Many

of these people perspire only with difficulty. In that case it is important to watch them carefully when in the hot box. Unless they begin to perspire I have them removed, because the intense heat may cause a rise in the body temperature and a heat stroke follow. I do not, as a rule, advise the use of diaphoretics, but if the patient cannot perspire a small dose of pilocarpin hydrochloride, $\frac{1}{10}$ of a grain, may be sufficient to start perspiration.

The type of nephroses that Epstein has described has nothing to do with the type that we are discussing here, and it does not come under the same category. They are differentiated by having marked lipemia with very high cholesterol in the blood. He claims remarkable results by keeping them on a high protein diet. Personally I have never come across a case in which the edema improved by high protein except where the chloride and salts were restricted. Dr. Christian's experiences in Boston have been similar to mine.

On the whole the edematous patients are comfortable and do not have any of the violent symptoms that we meet in the uremics. They may get fluid in the peritoneum, pleura and pericardium and usually die of secondary cardiac embarrassment or edema of the lungs.

The patients who have difficulty with nitrogen elimination usually run a stormy career, with violent headaches, nausea, vomiting, all kinds of nervous symptoms, varying in degree from restlessness and insomnia to absolute irrationality and coma. They may also have disturbances in the special senses, with diplopia, temporary blindness, retinitis, retinal hemorrhages, etc.

Bromides, chloral hydrate, cinchophene and sodium salicylate help control the symptoms tremendously. Venesection is of great value, and so is lumbar puncture.

In the later stages when coma has set in we very frequently get satisfactory results by doing a venesection, withdrawing 300 to 500 c.c. of blood, followed by a glucose infusion of 300 to 500 c.c. of a 5 to 6 per cent. solution.

Diaphoreses and purgation are also of great value.

The treatment of uremia at best is hopeless. All we can do is to delay the inevitable. Once the diagnosis of uremia is made it spells the patient's death sooner or later, usually sooner.

Therefore do I repeat what I said before: I consider every case of hypertension a potential nephritic, and every nephritic a potential uremic, and treat the uremia, not when it is with us and we are helpless, but months and years before, when we have every facility for its prevention.

TREATMENT OF TETANUS.

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Large doses of antitoxin have been rather commonly used in the treatment of tetanus. By reporting four consecutive cases which recovered following the use of large amounts of antitoxin intravenously, it is hoped to emphasize the value of this form of treatment.

The routine procedures adopted follow very closely those used by Woolf[1] in reporting a successful case.

1. Antitoxin is given in dosages of 10,000 to 20,000 units, intravenously, several times daily until all spasm is gone.

2. Morphin hypodermically and chloretone by rectum are given every four to six hours during the stage of reflex hyperexcitability.

3. Liquid nourishment and large amounts of water are given every two hours.

REPORT OF CASES.

Case I.—G. B., male, aged forty-three years. Admitted May 28, 1919.

Complaint. Abdominal pain and cramps.

Present Illness. Three weeks prior to admission he ran a splinter of wood in his finger. One week later he noticed stiffness of his jaw. Stiffness gradually extended to neck, arms, legs and abdomen.

Physical Examination. Temperature, 101.3°; pulse, 120; respiration, 28.

Patient restless and perspiring freely. Jaw muscles spastic and teeth can be separated about three-quarters of an inch. "Risor sardonicus," marked rigidity of neck, arm, leg and abdominal muscles. Tendon reflexes exaggerated. No pathologic reflexes. Marked reflex hyperexcitability.

Treatment. Routine procedure as above. Morphin, gr. $\frac{1}{6}$; chloretone, grs. xx every six hours.

Antitoxin. May 28, 10,000 units intravenously twice; 3000 units intramuscularly.

May 29, 30, 10,000 units intravenously twice.

May 31, 10,000 units intravenously three times.

June 1, 2, 3, 10,000 units intravenously twice.

June 4, 5, 6, 7, 11, 10,000 units intravenously once.

June 14, 15, 25, 10,000 units subcutaneously once.

Total antitoxin, 213,000 units.

June 25, discharged cured.

[1] Woolf: Jour. Am. Med. Assn., 1919, lxxii, 1266.

CASE II.—E. C., male, aged eight years. Admitted October 8, 1919.

Complaint. Stiffness of jaws and convulsions.

Present Illness. About one month prior to admission the child had gone barefoot and had stubbed its toe, leaving a slight abrasion which healed in about a week. Six days before admission he noticed stiffness of jaw, neck and back. On October 7 he had several convulsions.

Treatment. Routine as above.

Antitoxin. October 8, 30,000 units intravenously.
October 9, 10,000 units intravenously three times.
October 10, 10,000 units intravenously twice.
October 11, 10,000; 15,000 units intravenously three times.
October 12, 10,000 units intravenously three times.
October 13, 15,000; 20,000 units intravenously.
October 14, 20,000 units intravenously twice.
October 15, 16, 20,000 units intravenously three times.
October 18, 20,000 units intravenously twice.
October 19, 20, 20,000 units intravenously three times.
October 21, 10,000 units intravenously three times.
October 22, 10,000 units intravenously twice.
October 23, 24, 10,000 units intravenously.
October 25, 10,000 units; 20,000 units intravenously.
October 26, 27, 28, 29, 10,000 units intravenously twice each day.
October 30, 31, November 1, 10,000 units intravenously once each day.
November 1, developed urticaria.
November 27, discharged cured.
Total antitoxin used 755,000 units.

I am indebted to Dr. Blankenhorn for taking charge of this case and also for the use of a syringe outfit by means of which a small needle can be inserted into a vein, and the antitoxin, together with a small amount of saline, injected under pressure.

CASE III.—A. B., female, aged eight years. Admitted June 23, 1919.

Complaint. Stiff jaws.

Present Illness. Two weeks prior to admission the patient ran the point of an umbrella into her foot. Three days ago she suddenly became stiff all over and was unable to chew her food. The day before admission she had a convulsion.

Physical Examination. Temperature, 100.2°; pulse, 128; respiration, 26.

General rigidity; marked "risor sardonicus;" hyperactive reflexes; exalted reflex excitability.

Treatment. Routine procedure as above.

Antitoxin. June 23, 25,000 units intravenously.

June 24, 10,000 units intravenously twice.
June 25, 10,000 units; 5000 units intravenously.
June 26, 5000 intravenously; 15,000 units intravenously.
June 27, 10,000 units intravenously.
June 28, 10,000 units intravenously.
June 29, 15,000 units intravenously.
June 30, 15,000 units intravenously.
July 1, 12,000 units intravenously.
July 2, 15,000 units intravenously.
July 4, 5000 units intravenously.
July 6, 5000 units intravenously.
July 8, 5000 units intramuscularly.
July 10, 5000 units intramuscularly.
July 13, 5000 units intramuscularly.
July 16, 5000 units intramuscularly.
July 19, 5000 units intramuscularly.
July 23, 5000 units intramuscularly.
July 31, discharged cured.
Total antitoxin, 189,000 units.

CASE IV.—J. N., male, aged ten years. Admitted April 25, 1920.

Complaint. Sore and stiff foot.

Present Illness. Twelve days prior to admission the patient ran a nail into his foot. Nine days later the foot began to feel stiff and sore. On the day of admission his jaw became stiff and he had a convulsion.

Physical Examination. Temperature, 101°; pulse, 120; respiration, 30.

Muscles generally hypertonic, with a tendency toward opisthotonos. Jaws can be separated about one-half inch. Profuse perspiration. Marked "risor sardonicus." Deep and superficial reflexes exaggerated. Reflex hyperexcitability. No pathologic reflexes.

Treatment. Routine as in preceding case.

Antitoxin. April 25, 20,000 and 10,000 units intravenously.
April 26, 15,000 and 5000 units intravenously.
April 27, 15,000 units intravenously.
April 28, 15,000 units intravenously.
April 29, 15,000 and 18,000 units intravenously.
April 30, 20,000 and 20,000 units intravenously.
May 1, 20,000 units intravenously.
May 2, 10,000 units intravenously.
May 18, 5000 units subcutaneously.
May 23, discharged cured.
Total antitoxin, 188,000 units.

Discussion. *Statistics.* While it is the general opinion that antitoxin is of great value in the treatment of tetanus, it is extremely difficult to draw any definite conclusions as to dosage

or mode of administration from published statistics. The most comprehensive figures are those for the cases treated in the British Home hospitals during the years 1914–1917. These tables, compiled by Bruce,[2] and Cummings and Gibson,[3] were carefully reviewed by Ransome[4] and Golla,[5] who agree that no reliable conclusions as to the value of antitoxin can be drawn for the following reasons: (1) Prophylactic treatment modifies the disease by lengthening the incubation period which varies inversely with the mortality rate; (2) no attempt was made to standardize the size of dose, the method of administering or the promptness of treatment. For example, some of the cases reported by Bruce were as follows:

	No. of cases.	Mortality rate.
1914–1915	231	57.7
1916	100	31.0

It is impossible to be sure whether the lowered mortality rate was due to more efficient prophylaxis or because more antitoxin was used in the later series. However, clinically, the serum must have made a favorable impression, for in 1917 the British War Office ordered that 50,000 to 100,000 units be injected within the first few days after symptoms appear.

Method of Administration. Sherrington[6] has reported some experiments regarding the relative value of different routes in giving antitoxin. Monkeys were injected with eight times the lethal dose of tetanus toxin intramuscularly, and in forty-two to seventy-eight hours, tetanus antitoxin, 20 units per kilo, was injected with these results:

	Mortality rate, per cent.
1. Subcutaneous	92
2. Intramuscular	88
3. Intravenous	72
4. Intrathecal	44
5. Bulbar intrathecal	48
6. Cerebral subdural	100

These results would tend to show that for a given dose of antitoxin the intrathecal route was the most efficacious. However, at best, the mortality rate was very high and the results throw no light on the effect of the maintenance of a high concentration of antitoxin in the tissues by repeated injections.

Mode of Absorption of Tetanus Toxin. It is well known that tetanus toxin has a marked affinity for nerve tissue while the peripheral motor nerves have been proved to be the pathways by which it is conducted to the central nervous system. However, on experimental evidence there has been a controversy as to whether the toxin is conducted by means of the axis-cylinders or by the neural and perineural lymphatics. From a therapeutic standpoint it matters greatly as to which of these absorption paths is correct,

[2] Lancet, March, 1919, i, 9.
[3] Ibid.
[4] Ibid., December 2, 1917.
[5] Ibid.
[6] Ibid.

for obviously if tetanus toxin is conducted by the axis-cylinders only antitoxin can be of little value, while if the lymphatics carry it vigorous antitoxin therapy is indicated.

The work of Meyer and Ransome[7] seems to show that the conduction is entirely through the axis-cylinders. They showed that if tetanus toxin were injected subcutaneously in an extremity, and after some time the nerve of this extremity were removed and the extract injected into another animal, it would develop tetanus. However, Teale and Embleton[8] proved by reinjection experiments that after the injection of toxin in an extremity, within a short time, it is present in the blood, liver, spleen, etc., and even in the nerve of the opposite extremity, results which would be impossible if the toxin were conducted entirely by the axis-cylinders. In the same research it was demonstrated that blocking the neural and perineural lymph channels by the injection of iodin or colloids delayed the spread of toxin up the nerve. Furthermore, the experiments of Orr and Róus, confirmed by Teale and Embleton, showed that bacteria can travel along the neutral lymphatic sheath, thus inferring that tetanus toxin with its smaller molecule can do the same. Finally, Robertson[9] injected the peripheral nerve paths with Richardson's blue and found the lymphatics of the motor nerves to be much larger than in the sensory, which would help to explain the more ready conduction of tetanus toxin by the motor nerve paths.

Thus the latest evidence seems to point to at least a partial conduction of toxin by the lymphatic route. As a basis for therapy it would be safest to take the position that Robertson assumes, namely, that tetanus toxin appears in the blood stream and other tissues and can be neutralized by antitoxin at any stage in its passage before its final and relatively undissociable union with the ganglion cells. Consequently, the greatest indication for treatment is to maintain as high a concentration as possible of antitoxin in the blood and lymph stream. This can most readily be done by large and frequently repeated injections, intravenously. The small series of cases reported here would confirm somewhat the efficacy and harmlessness of this method of treatment.

Summary. 1. Four cases of tetanus are reported which recovered after receiving large doses of antitoxin intravenously.

2. War statistics of tetanus treatment by antitoxin are difficult to interpret because of the effect of prophylaxis.

3. Experimental evidence shows that tetanus toxin is at least partly conducted by the perineural lymphatics.

4. Theoretically the maintenance of a high concentration of antitoxin in the blood and lymph is indicated in tetanus treatment.

5. Practically, this may be accomplished by large frequent intravenous injections.

[7] Arch. Exp. Path. u. Pharm., 1903, xlix, 367.
[8] Jour. Path. and Bact., 1919, l, 23.
[9] Am. Jour. Med. Sc., 1916, cli, 31.

GONORRHEAL ENDOCARDITIS: REVIEW AND REPORT OF A CASE.

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It was seventeen years after Neisser had discovered the gonococcus and eleven years after Bumm had perfected the technic of demonstrating the organism before the gonococcus was proved to be the sole etiologic agent in a case of endocarditis. It had been observed several years before the discovery of the gonococcus that heart affections sometimes complicated gonorrhea. At this early date, when the etiology of gonorrhea was not known, the methods by which the complications were produced were in doubt except where *per continum* explained the process. Bumm first contended that the gonorrheal process was limited to mucous membranes. Finger later asked the question if the secondary processes associated with gonorrhea were due to the gonococcus. He answers the question by saying that these processes may be (*a*) purely gonorrheal; (*b*) pyogenic organisms entering the body through the diseased mucous membrane or lodge at the areas which have been damaged by the gonococcus or the products of its growth; or (*c*) purely toxic.

In 1896 Thayer and Blumer reported a case of endocarditis which they proved was purely gonorrheal in nature. Thayer and Lazear reported another case in 1899. Since these reports a fair number of undoubted cases of purely gonorrheal endocarditis have been reported. Standard text-books on pathology and medicine have for a number of years given the gonococcus an important place in the list of organisms producing endocarditis.

The above-mentioned reports were the first to prove definitely that the gonococcus did not limit its affections to the mucous membranes. The percentage of cases of gonorrhea in which there is a septicemia is probably higher than is usually thought. It is not unlikely that the diplococcus in the blood will in a certain number of cases cause only transient symptoms, such as fever, chill and albuminuria; but in others, due to some abnormality in the local tissue or to some special property of the strain of gonococcus, there will develop metastatic lesions.

The process by which the gonococcus lodges on the heart valves and produces endocarditis is probably very similar to the process by which any other organism lodges there. A septicemia is essential. It is generally thought that the organisms lodge directly on the valves along the line of closure, this line of closure being just back of the free edge of the valve. The bacteria are thought by some to be mechanically caught along the line of closure. Rosenow has disputed the above and claims that the bacteria get to the valves

by way of the capillaries as emboli. However, it has been proved (Coen and von Langer) that capillaries do not extend out as far on the valve as the line of closure. A previously diseased valve is thought to play an important role in the developing of an endocarditis. The roughened or thickened valve or endocardium predisposes to the bacteria lodging and multiplying here.

It is an interesting fact that gonorrheal endocarditis occurs on the right side of the heart in about one-third of the cases. In the thirty-two cases of Thayer and Lazear, 32.2 per cent. had the lesion on the right side of the heart. The recent work of Wherry and Oliver offers a plausible explanation of this fact. They found that the gonococcus grew much more abundantly when the carbon dioxide tension was slightly increased at the expense of the oxygen tension. Thus the conditions in the right side of the heart would be more suitable for the growth of the gonococcus.

Gonorrheal endocarditis occurs more often in the male than in the female about two to one. It most often occurs in early adult life, that is, in the twenties. The time of its occurrence in reference to the primary infection is variable. Some cases have occurred a few days after onset of primary infections while others have occurred late in the attack in persons who have had gonorrhea many times before.

There are two varieties of gonorrheal endocarditis: first a benign type and second a malignant type.

There is not much known definitely about the pathology of the first type, since this type very rarely comes to autopsy. It is entirely possible, though, that the toxin from the gonococcus can cause valvular changes. This is a sclerotic process. There is included under the benign type those infective cases which cause only slight inflammation in the endothelium, and possibly at times small verrucose vegetations are formed. These make up a certain percentage of the cases which show generalized symptoms and signs following gonorrhea. In cases of this kind a murmur at some stage of the disease can often be demonstrated. A positive blood culture may be obtained, but this alone is not conclusive evidence of an endocarditis. It seems that in a number of reports on this subject too much emphasis is placed on finding the gonococcus in the blood. This benign type may resolve with little damage or may progress to second type.

The second, or malignant type, of gonorrheal endocarditis has been studied more thoroughly because these cases usually come to autopsy. It is the tendency of the gonococcus to cause this second type of endocarditis. McCallum says ". . . the gonococcus is likely to give rise to large vegetations, which grow rapidly and are found in a crumbly soft state. Occasionally they are so massive as practically to occlude the whole valvular orifice. . . . a hint as to the nature of the infection may be gained from its frequent

occurrence in the valves of the right side of the heart, and from the rapid destruction of the valves themselves, so that one frequently sees great thrombus masses flopping back and forth on the end of a thread of tissue, which is all that remains of the valve."

The thrombotic vegetation begins as a small verrucose vegetation composed of new connective tissues, some wandering cells, mostly polymorphonuclears and gonococci. Fibrin and other elements of blood are deposited on this. The valve leaflets may be almost entirely destroyed by ulceration. The mural endothelium, most often contiguous to the valve, is usually more or less involved. This is usually the verrucose type. Infected emboli are frequently set free in the blood and metastatic lesions are often produced.

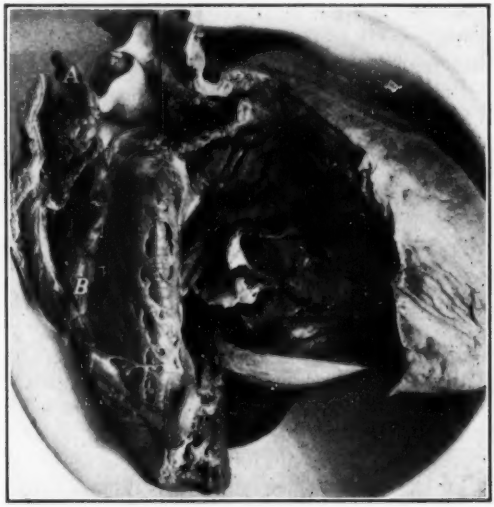

FIG. 1.—Pulmonary valve. Note destruction of left leaflet and the large thrombus attached to right leaflet, *A* to *B*.

For data relating to history and clinical findings the case here reported is cited.

As to treatment nothing specific can be mentioned. The general principles involved in treating any case of endocarditis should be carried out. If a focus of infection, as prostatitis or abscess is present, these should be properly treated. Substances given intravenously, like colloidal silver, have not given sufficiently satisfactory results in endocarditis to be recommended. In the chronic or subacute cases gonorrheal vaccines may be advisable.

CASE REPORT. Medical, No. 4616 (University of Virginia Hospital), male, white, aged twenty-eight years, admitted December 24, 1917.

Complaint. "Abscess in the liver."
History. (Summary).
Family History. Good.
Past History. Unimportant.

Present Illness. The patient passed the medical examination for the army in August, 1917. For some time before this he had complained of weakness, loss of appetite and pain in the stomach, after eating. In August he had urethritis (definite date not given) with no urologic complications. About the middle of September, 1917, began to have chills, these usually occurring during the afternoon or at night. They lasted from one to three hours and were followed by fever and sweats. Quinin in whisky seemed to stop the chills but did not prevent their recurrence. This condition continued, with slight improvement, until December 1, 1917, when the patient attempted to go back to work. He was forced to quit work at the end of the third day on account of a general swelling of his body and shortness of breath. He was advised by his home physician to go to bed, which he did not do, but walked about his room until coming to the hospital. Four days before admission he was told that he had a liver abscess.

Physical Examination. Poorly nourished white man, about thirty years of age, in a bed, on backrest, dyspneic on slightest exertion. Does not answer questions readily but is conscious; has spells of hiccoughing lasting from a few to several minutes. Skin is pale and has a lemon tint. Conjunctivæ are pale and have slight yellow tinge. Routine examination of eyes, ears, nose, mouth and throat negative; face not swollen. Cervical, axillary and inguinal glands palpable. Moderate pitting on pressure about ankles. Left knee-joint shows a small amount of swelling, slight or no tenderness; patella not floating; some fluctuation on the side of the patella. Knee-jerks normal.

Chest is asymmetrical, due to bulging of the eighth, ninth and tenth ribs on the right side. Lungs are resonant throughout; a few moist rales at bases behind. On examination of the heart a forcible cardiac impulse is seen in the fifth interspace and extending outward as far as the nipple line; the apex-beat is felt in the fifth interspace outside the left midclavicular line; no thrills felt. Percussion reveals that dulness extends 1 cm. to the right of the right sternal border. On auscultation a double murmur is heard more forcibly in the third left interspace near the sternal border, also quite readily at the pulmonic area. The systolic murmur is heard faintly at the apex. Both are rather low pitched, and the systolic is harsh in quality. The rate is 84 per minute. About every eighth beat is dropped. Blood-pressure is $\frac{125}{63}$. The abdomen is not distended; no dulness in flanks. Liver dulness extends in anterior midclavicular line, 2 cm. below the costal margin; edge not palpable; some tenderness over the liver. Spleen not palpable.

Genitalia apparently normal; no sores; no urethral discharge.

Laboratory Findings. On admission the leukocyte count was 15,000. Smear negative for malaria. Later findings in blood were: Leukocyte count, 17,300; red count, 3,590,000; hemoglobin, 45 per cent. (Dare); differential shows polymorphonuclear leukocytes 95 per cent.; lymphocytes, 2.5 per cent.; large mononuclears, 2 per cent.; transitionals, 5 per cent.; eosinophiles, 0 per cent.; smears were again negative for malaria; reds show a slight degree of poikilocytosis and anisocytosis; blood cultures negative (5 c.c. blood in 50 c.c. of glucose broth). Urinalysis: 800 c.c.; amber; 1020; acid; 1 mm. ring albumin; sugar negative; hyaline; finely granular; coarsely granular; pus and epithelial casts; 10 to 15 pus cells to high power field; few reds; bile positive. Daily urinalysis showed about the same as the above.

For temperature, pulse and respiration see chart.

Impressions. Ulcerative and vegatative endocarditis, probably of aortic valve because of the relative infrequency of pulmonic endocarditis.

December 25. Patient's condition unchanged. Had severe chill, lasting fifteen minutes, followed by profuse perspiration. Treatment consists of rest in bed; water freely; liquid diet; ice-bag to pericardium; tincture digitalis (fat-free), ℳxx t. i. d.; morphin sulphate as sedative.

December 28. Perspires freely; vomited after nourishment; general condition poor; physical findings unchanged.

December 29. Patient irrational.

January 5. Condition of patient has gradually become worse; hiccoughing at intervals; skin cold and moist; pulse weak and irregular; breathing labored; lungs filled with moist rales and patient is in a profound stupor. Heart findings are the same as above except that the heart dulness extends 3 cm. outside the left midclavicular line.

January 5, 5 P.M. Respiration ceased.

Autopsy Report (three hours after death).

Pathologist. Dr Harry T. Marshall.

Anatomical Diagnosis. Gonococcal endocarditis and septicemia; ulcerative and vegetative pulmonic endocarditis; ulcerative aortic endocarditis; mural endocarditis; milky patch over the epicardium. Old pleural adhesions near the right diaphragm; puckered scar at the apex of the right lung; infarcts in lungs; thrombi in branches of pulmonary artery. Fatty degeneration of the intima of the aorta. Acute papillary nephritis; cloudy changes in kidneys; anomaly of right kidney. Fatty liver. Accessory spleens. Adenoma and hypertrophy of thyroid.

Heart. Muscle is very soft and pale. A large milky patch over the upper anterior surface of the right ventricle. On section the muscle is soft, opaque and cloudy. Right ventricle is distinctly distended. Tricuspid clear. A fresh chicken-fat clot fills the right

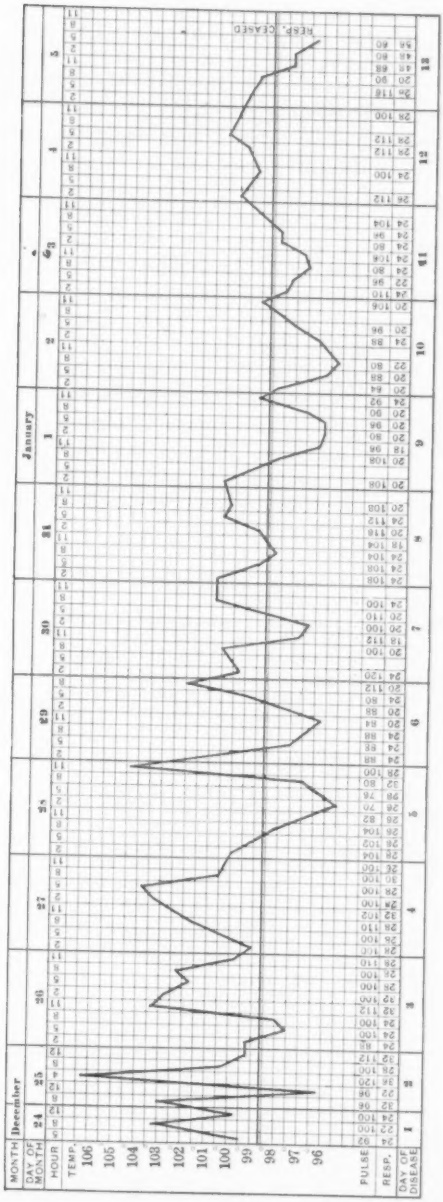
MONTH
December
January
DAY OF MONTH
HOUR
TEMP.
PULSE
RESP.
DAY OF DISEASE
RESP. CEASED

FIG. 2

ventricle and extends to the pulmonic valve, which also shows pronounced destruction from endocarditis. The left leaflet is almost completely eroded, only a few vegetations representing it. The right leaflet is buried in a thrombus, and this thrombus is cone shaped and furrowed in contour and extends at least three-quarters of an inch into the pulmonary artery; it is attached at its base to the valve leaflet. Below the valve small mural vegetations are covered with an elastic, recent clot continuous with the clot found in the right ventricle on the one hand, and with the valve thrombus on the other. Posterior leaflet of aortic valve shows a small ulceration and evidence of a slight chronic thickening. Otherwise the valves are clear except for a few verrucose vegetations on the aortic valve.

Smears from thrombi and heart's blood show Gram-negative, intracellular, biscuit-shaped diplococci.

Cultures from the heart's blood and from thrombi negative.

The diagnosis in this case is based on a recent history of gonorrhea, negative cultures, morphology of organism in smears and the character of lesions found at autopsy. None of the above findings alone would be sufficient for making a diagnosis of gonorrheal endocarditis, but when taken together they prove beyond a doubt that the gonococcus is the etiologic factor.

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EPIDEMIC ENCEPHALITIS: OBSERVATIONS ON A SERIES OF FIVE CASES; AUTOPSY FINDINGS; PREDOMINATING SYMPTOMATOLOGY; RELATION TO INFLUENZA; PERSONAL CONCLUSIONS.

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and

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new york.

During the fall, winter and spring of 1918–1919, and again in 1919–1920, there have been reported from numerous sites in the United States a number of cases clinically known as epidemic encephalitis. The relative frequency of the disease is shown by the ever-increasing number of cases and case reports that are published in the medical literature. The earliest observations in this country were those of Peter Bassoe, Josephine Neal, F. A. Ely, B. Sachs, P. Wegeforth, J. B. Ayer and others, and since followed by those of F. Tilney and H. A. Riley, L. F. Barker and E. Cross and S. Irwin, etc. The predominating symptomatology, as reported by the above observers, has been markedly consistent, probably the best recognized of which are the lethargic state, the frequency of cranial nerve involvement, the spinal fluid findings and the relative frequency with which the disease is preceded by influenza. Our own experience with the disease dates from October, 1918 (Case I). Since that time we have had the opportunity of carefully studying four additional cases, the entire series of which follows:

Case Reports These cases are from the Medical Wards of the Roosevelt Hospital, New York City, N. Y.

Case I.—S. W., child, aged five years. Admitted October 24, 1918. Service of Dr. Rowland G. Freeman. Previous history of influenza.

History. Chief Complaint. Child is irrational and irritable; very restless.

Present Illness. About four days ago the patient, having just recovered from an attack of influenza and bronchopneumonia, was well enough to be up and play around the house. For two days the child appeared well and normal in her actions and was very bright and active. Two days ago there was a marked change in the child's disposition. She became irritable and then irrational, and within twelve hours was so much so that she did not recognize her grand-

mother. The patient was unable to articulate properly and did not seem to understand when spoken to. Did not complain of diplopia.

Past History. Usual childhood diseases; influenza. Otherwise always well.

Family History. Negative.

Physical Examination. Temperature, 102°; feeble pulse, 100; respirations, 24. Well-nourished child, restless, tossing about the bed; moderate opisthotonos. Rolling of the eyes. Face expressionless. Marked masked appearance.

Head. Moderate opisthotonos. Pupils equal, regular and react to light and accommodation. There is a marked nystagmus of both eyes in all directions; no strabismus; no ptosis; no diplopia. Fundi normal. Ears, nose and mouth negative except for enlarged tonsils.

Heart and Lungs. Negative.

Abdomen. Superficial reflexes exaggerated; otherwise negative.

Extremities. Knee-jerks equal but hyperactive (4 plus). Kernig, negative. No Babinski; no ankle-clonus. Romberg, 2 plus.

Laboratory Findings. Urine: Specific gravity, 1020; albumin, none; sugar, none. Few white blood cells and epithelial cells.

Blood. White blood cells, 22,000; polynuclears, 64 per cent.; lymphocytes, 36 per cent.; red blood cells, 4,500,000; hemoglobin, 80 per cent. Von Pirquet test, negative.

Spinal Fluid. Clear, normal pressure, eleven cells; 100 per cent. lymphocytes. Cultures, sterile. Smear, no organisms. Wassermann, negative. Globulin 1 plus. Colloidal gold curve, 1.2.2.1.1.1.1.2.0.0.

Course. Patient was intermittently stuporous and restless. Showed first sign of awakening mental activity on November 12, 1918, nineteen days after onset. From this time on mental condition became rapidly brighter. Child began to take nourishment and showed an interest in her surroundings. The normal facial expression reappeared and the nystagmus of the eyes was absent on November 15, 1918. The child was allowed out of bed on November 18, 1918, and it was then found that she had lost all power to use her lower extremities and could not walk or even stand up unassisted. This flaccid paraplegia of the lower extremities was very persistent, and there was also a marked diminution of the muscle strength of the left arm and hand. Even with returning muscular power the child seemed to have forgotten how to walk and had to be actually taught, first crawling about on hands and knees and then slowly toddling about like a child of one year. She was discharged absolutely cured, with normal use of all extremities on December 15, 1918.

Case II.—K. H., housewife, aged thirty-nine years. Admitted February 5, 1920. Service of Dr. John S. Thacher. Previous history of influenza.

History. Present Illness. Patient admitted in condition of lethargy. Sent into the hospital with a diagnosis of meningitis, but showed none of the ordinary symptoms. Seemed to be in possession of all her mental faculties except that she took absolutely no interest in her environment. When engaged in conversation her replies were either "Yes" or "No" or some other monosyllable. She has been in this condition for fourteen days, more marked for the past seven days.

Past History. About one month ago the patient had influenza, which merged into this condition. At the onset of the attack she had severe headaches, mostly frontal, at times occipital; sore-throat and pains in the back. Her temperature was 101° F. Her pulse was never above 80. Twitching of the hands and face, mostly on the left side. Transient systolic heart murmur at base. Patient was never in this condition before.

Family History. Negative; married; children all healthy; nothing like this in family before.

Physical Examination. Temperature, 102° F.; respiration, 20; pulse, 80. A rather large, fleshy, but not obese woman, resting quietly in bed, breathing quietly and regularly. Patient conscious but takes absolutely no interest in her surroundings. Said to be slightly disoriented but not apparent on admission. There is no marked blankness to the facial expression.

Head. Pupils small, moderately contracted, but react to light and accommodation. Marked ptosis of the left lid and slight ptosis of the right lid. Eye movements not coördinated. Right eye shows moderate external strabismus. Disks do not stand out sharply, less white than usual, but not definitely abnormal. No nystagmus.

Neck. No glands. Thyroid, negative.

Chest. Breasts negative. Lungs, clear. Heart, negative. Slight systolic murmur at apex.

Abdomen. Liver and spleen not palpable. Superficial abdominal reflexes present and of normal intensity.

Extremities. Muscle strength essentially normal. Left knee-jerk more active than right. No Babinski or modifications. No Brudzinski. Slight suggestion of a Kernig.

Laboratory Findings. Urine: Negative throughout. Temperature on admission, 102° F. First week between 99° and 101° F.; second week between 98° and 100° F.

Blood. White blood cells, 12,200; polynuclears, 76 per cent.; lymphocytes, 24 per cent.; culture, sterile; Wassermann, negative; blood-pressure, 98/72. Widal, negative.

Blood Chemistry. N. P. N., 32.90; urea nitrogen, 15.9; uric acid, 2.10; creatinin, 0.91; sugar, 0.09.

Phenolsulphonephthalein Test. 60 per cent. dye elimination in two hours.

First Spinal Fluid Examination. February 6, 1920. Clear, normal pressure. Eighty-one cells per cubic millimeter; 100 per cent. mononuclears. Culture, sterile. Smear, no organisms. Wassermann, negative. Globulin, 1 plus. Colloidal gold curve, 0.0.0.1.1.2.1.0.0.

Second Spinal Fluid Examination. March 2, 1920. Clear, normal pressure. Eight cells per cubic millimeter; 100 per cent. mononuclears. Wassermann, negative. Culture, sterile. Smear, no organisms. Globulin, 1 plus. Colloidal gold curve, negative.

Course.

February 5. Semicomatose all day.
9. Condition unchanged.
11. Slightly irrational. Ptosis of lids were marked.
14. Not so lethargic—awake for several hours.
16. Markedly brighter mentally.
29. Patient continues to improve. Facial expression has returned. Begins to show conversational interest in her surroundings. Ptosis of eyelids less marked. External strabismus of right eye now gone.

March 5. Mentality normal. Ptosis of right lid gone. Ptosis of left lid much less marked. Facial expression animated and bright.
6. Discharged cured.

CASE III.—E. L. G., child. Service of Dr. Rowland G. Freeman. No previous history of influenza.

History. Chief Complaint. Diplopia, headache, frontal and occipital, dizziness, duration twelve days.

Present Illness. Nineteen days ago patient started to complain occasionally of being dizzy and having pains in the head. His father noticed his eyes did not "look quite right," and once or twice, when walking, he stumbled into objects, furniture, etc. In the morning, while apparently well and getting ready for school, he told his father he had two neckties on. This was the first time they had noticed any diplopia. For the next seven days, slowly but progressively, the child became mentally duller. At first it was hardly noticeable, except to his parents. Ten days ago he went to school for the last time. He left home in good spirits and returned from school as though walking in a trance. He was put to bed at once and a physician was called. He was pale, breathing quietly, and his pupils were dilated. At this time the child could not be aroused. The next morning he was awake and considerably brighter, but still very listless. He has been better at times, but up until the day of his admission to the hospital he was always lethargic. Occasionally he would rouse and speak with intelligence and take an interest in his surroundings. On two occasions, one night and five nights

before admission, he twitched as he lay in his stupor. This twitching was confined chiefly to the left side. The face and hands were chiefly involved. In the morning of the day of his arrival at the hospital he was fairly bright, took an interest in his family, the snow storm and the automobile ambulance. Soon after admission he sank into a stupor and remained that way. He could be aroused, but would not reply to questions. From the day of his return from school the child has taken only liquid food. He is unable, apparently from lack of desire, to chew even the smallest pieces of food. In his markedly depressed periods he will not rouse or take food or water.

Past History. Tonsillitis one year ago. Appendicular colic at times. Has had measles, whooping-cough and chicken-pox.

Family History. Father and mother living and well. One brother living and well. No history of fainting spells in the family. No tuberculosis, cardiorespiratory or chronic disease in the family.

Physical Examination. Temperature, 99.6° F.; pulse, 100; respirations, 24.

General. A thin but well-developed lad of nine years, resting quietly in bed. Takes no interest in his surroundings. Does not speak when spoken to except in monosyllables. There is a blank facial expression.

Head. Any sudden bright light will cause him to turn his eyes away but not his head. Teeth good. Tongue coated. Pharynx hard to see because of lack of coöperation, but apparently negative. Eyes: Pupils moderately contracted, equal, react to light and accommodation. Fundi negative. Movements are not coördinated. Slight external strabismus of right eye. No nystagmus.

Neck. Slightly stiff (of muscular and not meningeal origin). When the head is flexed it maintains position until muscular fatigue causes it to drop back on the pillow gradually.

Chest. Heart and lungs negative.

Abdomen. Superficial abdominal reflexes present but not exaggerated. Liver and spleen normal.

Extremities. When placed in one position they remain there until muscular fatigue lowers them (catatonia). Back stiff (muscular resistance). Brudzinski sign present. Babinski suggestive in left foot but not in right. Knee-jerks present and equal. Reinforced Babinski negative. Bilateral Kernig positive.

Laboratory Findings. Urine: Straw-colored; acid reaction; specific gravity, 1020; no albumin; no sugar; no red blood cells; a few white blood cells. Acetone and diacetic absent. Throughout sickness it varied but little from this.

Blood. Pressure 112/70. White blood cells, 10,200; polynuclears, 74 per cent.; lymphocytes, 26 per cent.; Widal (−). Throat culture, negative. Schick test, negative. Von Pirquet, negative; Wassermann, negative.

First Spinal Fluid Examination. Day of admission. Clear, normal pressure; 43 cells, 96 per cent. mononuclears. Cultures, negative. Smear, no organisms. Spinal fluid Wassermann, negative. Globulin, 1 plus. Colloidal gold curve, 0.0.1.1.2.0.0.1.0.

Course. Patient continued in his lethargic condition for seven days. Would rouse and speak in monosyllables when shaken. The blank facial expression was marked. Muscular rigidity of left arm and leg persisted. On the eighth day after admission patient began to show an interest in his surroundings. There was a gradual diminution in the lethargy. On the fourteenth day the spasticity of the left arm and leg was gone and there was a marked improvement in the facial expression. Patient was discharged on the twentieth day entirely well. A second spinal fluid examination on the tenth day gave the same findings as the first one.

CASE IV.—E. F., male, aged forty-two years. Admitted February 12, 1920. Service of Dr. Evan Evans. History of influenza.

History. Chief Complaint. "Nervousness." Sudden onset. One week's duration.

Present Illness. Two weeks ago the patient developed influenza. This cleared up in about one week. Patient then gradually became exceedingly "nervous," and this condition has grown progressively worse. There has been also a general feeling of malaise and drowsiness for the past three days. No diplopia. No subjective ataxia. No headache. Appetite poor. Bowels regular.

Past History. No previous illness. Chancre and gonorrhea denied.

Family History. Negative.

Physical Examination. Temperature, 98.8° F., pulse, 90; respirations, 24.

Head. Eyes, pupils equal, regular and react to light and accommodation. No strabismus. No ptosis. No nystagmus. No diplopia. Nose, ears and mouth negative. Fundi negative.

Neck. Negative.

Thorax. There is a marked myotatic irritability of the somatic muscles of the arms and thorax.

Heart and Lungs. Negative.

Abdomen. Liver and spleen not palpable. No masses; no tenderness. Superficial abdominal reflexes greatly increased; marked myotatic irritability and lateral to-and-fro twitchings of the abdominal muscles.

Extremities. Knee-jerks equal but hyperactive (4 plus). Romberg test, markedly positive. Kernig test, negative. Brudzinski, negative. No ankle-clonus. No Kernig.

Positive Findings on Admission. Ataxia of both legs. Myotatic irritability of muscles of arms, thorax and abdomen and to-and-fro twitchings of abdominal muscles. Drowsiness.

Laboratory Findings. Urine: Acid, 1028; albumin, a trace; no sugar; few white blood cells.

Blood. White blood cells, 8200; polynuclears, 78 per cent.; lymphocytes, 22 per cent.; hemoglobin, 85 per cent.; red blood cells, 4,800,000. Wassermann, negative. Pressure, 140/90.

First Spinal Fluid Examination. February 14, 1920. Clear, normal pressure. Seven cells, 100 per cent. mononuclears. Culture, sterile. Smear, no organisms. Wassermann, negative. Globulin, 1 plus. Colloidal gold curve, 1.2.2.4.4.4.3.3.0.

Second Spinal Fluid Examination. February 25, 1920. Clear, normal pressure. Seven cells, 100 per cent. mononuclears. Culture, sterile. Smear, no organisms. Wassermann, negative. Globulin, 1 plus. Colloidal gold curve, 5.5.4.3.3.3.3.2.0.

Blood Chemistry. N. P. N., 32.50; urea nitrogen, 15; uric acid, 1.8; creatinin, 0.9; sugar, 0.11; carbon dioxide, 50.

Course. February 25, 1920. From the time of admission the patient became very listless and drowsy, with sudden irrational outbursts. The speech, which was quite coherent on admission, is scarcely intelligible, and is jerky and mumbled. Patient more stupid.

Eyes. Pupils unequal. Right larger than the left. Both react to light. Tongue deviates to the left; marked tremor of eyelids, lips, muscles of expression and hands upon executing any movements of these.

Neck. Somewhat stiff.

Heart and Lungs. Still negative. Myotatic irritability, 4 plus. Reflexes of upper extremities, 3 plus. Reflexes of lower extremities, 3 plus. Babinski, negative. No clonus.

These findings persisted unchanged. There was a noticeable absence of the "mask face" appearance, found in all of the other cases. The lethargic element was markedly present and remained until the death of the patient on March 3, 1920.

Autopsy Findings. Postmortem of E. F., aged forty-two years.

Died March 3, 1920.

Autopsy, March 4.

Autopsy performed by Dr. Rolfe Floyd at Roosevelt Hospital.

Clinical Diagnosis (Medical Division): Encephalitis lethargica.

Anatomic Diagnosis. No cause of death in gross.

Chronic nephritis (slight).

Edema and congestion of lungs.

Old pulmonary scar.

External Examination. Body of an adult, white, male, very emaciated; rigor mortis moderately developed. No edema; superficial nodes not felt. Eyes, ears and nose normal. External genitals normal. No evidence of status lymphaticus except a wide pelvis. Subcutaneous fat much reduced and very yellow. Muscles very red; all tissues dry; blood volume small.

Internal Examination. Peritoneal cavity is normal.

Vault of diaphragm is at fourth space, right and left.

The right pleural cavity contains no fluid. There are some moderately firm adhesions over the upper lobe.

The left pleural cavity is normal.

The right lung shows some congestion and edema and a few hemorrhagic spots in the lower lobe, which resemble agonal hemorrhages; no gross consolidation; a very little purulent bronchitis of the small tubes.

The left lung shows the same condition, but there is, in addition, a puckered scar in the upper part of the left lower lobe, and about this the bronchi contains more pus of foul odor.

The large bronchi of both lungs are moderately congested and coated with a little mucopus; the hilus nodes are normal, no old tuberculous foci being found in them.

The larynx and trachea are normal.

The thyroid gland is normal, the thymus not recognizable.

The pericardium is normal except for a hemorrhagic spot under the visceral layer, about 5 cm. in diameter.

Heart is normal in size, valves, walls and coronaries.

Tongue, pharynx and *esophagus* normal.

Stomach mucosa shows an acute, patchy congestion of only moderate grade.

Small gut shows marked congestion of the upper jejunum, otherwise normal.

Large gut normal except for a small pin-head ulcer in the sigmoid. The rectum contains a large mass of soft feces, perhaps a pint, while the rest of the large gut is comparatively empty.

Nodes of mesentery are large, white and flat, the largest being 1 cm. across.

Liver normal, weighs 1500 grams.

Gall-bladder normal.

Spleen normal, weighs 180 grams. Follicles can be seen.

Pancreas normal.

Suprarenals normal.

Kidney very dark red, smooth, with a decidedly adherent capsule. On section the dark color is very evident but the markings are pretty good and the glomeruli can be seen. In one kidney there is a whitish nodule 2 mm. across in the cortex which looks like a fibroma.

Pelves, ureters, bladder and *prostate* normal.

Pia is a little congested and looks a little dry. There is a slight adhesion to the dura over the tip of the left temporosphenoidal lobe.

Cortex normal except for a slight area, about 1 cm., across which is soft and yellow over the outer aspect of the right temporal lobe.

Centrum ovale normal.

Ventricles, ependyma and *choroid plexus* normal.

Basal ganglia normal except that the vessels paths can be traced as white grooves after wiping the cut surface with knife. At the back of the left thalamus the vessels after section show like small dark pits, but this appearance cannot be called hemorrhagic.

The cerebellum, pons and *medulla* are normal.

Cerebral arteries normal.

Pituitary normal.

Ethmoid, frontal and *sphenoid sinuses* normal.

Middle ears normal.

Venous sinuses of dura normal.

MICROSCOPIC LESIONS OF E. F.

Lung 1. Congestion, edema and bronchopneumonia. The ordinary picture of edema and congestion, and is associated with peribronchitic zones of pneumonia which vary much in size and in which the chief component of the exudate is pus. A secondary bronchopneumonia.

Lung 2. Similar to "1," but the pneumonia is insignificant and there are areas in which the spaces are filled with blood; very likely agonal.

Lung 3. Interstitial pneumonia; from the scarred region. There is much fibrous tissue, with congested vessels and one area of hemorrhage. The wall of a damaged bronchus, probably dilated, is made of vascular granulation tissue which completely replaces all the layers of the normal wall. Some remnants of the epithelium are left. There is nothing in the section to mark the original process as tubercular, and it may well be the result of a long postbronchopneumonia.

Tongue. Circumvallate papillæ normal.

Liver. Slight acute congestion, somewhat patchy in distribution.

Spleen. Normal.

Pancreas. Normal. Islands hard to find.

Kidney 1, 2, and 3. Acute congestion, moderate. No connective tissue anywhere to explain the adherent capsule.

Thyroid. Normal.

Mesenteric Nodes. Normal. Rather too many long connective-tissue nuclei in the sinuses and one follicle shows a lighter center with big endothelial cells in it.

Retroperitoneal Node. Chronic adenitis. There is a definite inflammatory growth of connective cells and fibrillated ground substance in the lymph sinuses. The vessels are overful of blood.

Cortex and Pia 1. Normal. From vertex normal except for rather an excess of cells on the pial surface. These are not evenly distributed and are not seen in the meshes of the arachnoid. There is no perivascular exudate in the cortex.

Cortex and *Pia* 2. Cortical softening. From yellow softened area. There is a pathologic expression in the line of the cortex into

which the arachnoid dips. The cortex in this region shows an uneven margin, looser neuroglia than normal and a complete absence of pyramidal cells. In the overlying arachnoid are many elongated connective-tissue cells filled with yellow pigment.

Centrum Ovale. Encephalitis. A distinct round-cell infiltration along one vessel. Some light purple homogeneous rounded masses are scattered about. Significance unknown.

Left Optic Thalamus. Encephalitis. An extremely marked lesion showing massive perivascular round-cell exudate about many vessels. Few round cells lie even along the capillaries. Some vessels show none, some very few. Others seem to be nearly obliterated by the massive exudate. Often the exudate encircles both artery and vein running side by side. Sometimes some red cells lie outside the vessel walls among the round cells; in one instance only is there a very minute hemorrhage which goes beyond the perivascular lymph space. There are many globules of hyalin light purple substance, sometimes scattered along a diseased vessel. They may be brain sand. There seems to be an excess of round cells all through the tissue, but this is difficult to determine. The inflammatory cells run strictly true to type, no polynuclears being seen.

Right Thalamus. Encephalitis. Same lesion as shown above, perhaps not quite so pronounced.

Left Caudate Nucleus. Normal. Some vessels show a few too many cells in their outer coat, but without the lesion found elsewhere these would be passed is incidental and without pathologic significance. The ependyma is normal.

Right Caudate Nucleus. The perivascular infiltration, though much less than in the thalami, is distinct and characteristic.

CASE V.—E. M., male, aged twenty-three years. Admitted May 26, 1920. Service of Dr. A. E. Sumner. No previous history of influenza.

History. Chief Complaint. Sleepiness. Headache. Diplopia. Onset gradual. Duration three weeks.

Present Illness. About three weeks ago patient had an occipital headache and also some indefinite pain in the epigastrium. This disappeared, but the headache returned and has remained constant. Two weeks ago the patient began to have difficulty in vision, could not read letters and could not see objects distinctly, held near to him. He then noticed that an object would appear double to him, *i. e.*, diplopia, and this symptom has persisted. He has been very sleepy since the onset, so much so that he can sleep for twenty-four hours in succession without any desire to awake. There has been no stiffness of the neck, no vomiting, no cardiac or respiratory symptoms.

Past History. No previous illness. No history of influenza or pneumonia. Chancre one year ago; gonorrhea denied.

Family History. Negative.

Physical Examination. Temperature, 99.6°; pulse. 80; respirations, 20. Patient lying quietly in bed and apparently in a sound sleep.

Head. Marked absence of normal facial expression and appearance of the so-called "mask face."

Eyes. Both pupils irregular, react sluggishly to light, but normal to accommodation. There is a fine lateral nystagmus of both eyes. Spasm of right eyelid and suggestion of ptosis. Marked diplopia. No strabismus. Fundi, normal.

Nose, Ears and Mouth. Negative.

Neck. No stiffness; no masses.

Thorax. Lungs. Negative.

Heart. Negative.

Abdomen. Spleen and liver not palpable. No masses; no tenderness. Superficial abdominal reflexes normal.

Extremities. Knee-jerks very sluggish but equal. No Babinski. No ankle clonus. Brudzinski sign absent. Romberg, negative. Kernig, negative.

Laboratory Findings. Urine: Acid; 1032. No albumin. No sugar. Occasional white blood cells.

Blood. White blood cells, 8400; polynuclears, 77 per cent.; lymphocytes, 23 per cent.; red blood cells, 4,800,000; hemoglobin, 88 per cent.; Wassermann, negative.

First Spinal Fluid. May 26, 1920. Clear; normal pressure; forty-three cells; 100 per cent. mononuclears. Spinal fluid Wassermann, negative. Globulin, 1 plus. Culture, sterile. Smear, no organisms. Colloidal gold curve, 1.1.3.3.3.2.1.0.0.

Second Spinal Fluid. May 28, 1920. Findings same as in first lumbar puncture except that thirty-six cells, 100 per cent. mononuclears. Colloidal gold curve, 1.1.3.4.4.3.2.1.0.

Third Spinal Fluid. June 2, 1920. Findings same as first and second lumbar punctures except that nineteen cells, 100 per cent. mononuclears. Colloidal gold curve, 0.1.1.3.3.3.2.1.0.

Blood Chemistry. N. P. N., 35.6; urea nitrogen, 16; uric acid, 1.9; creatinin, 0.9; blood sugar, 0.13.

Course. The patient ran an uneventful course. He continued lethargic, with the above physical findings until June 3, 1920. From this time on the lethargy gradually disappeared and on June 7, 1920, patient was out of bed. The diplopia disappeared by June 5 and by June 10 the pupils reacted normally to light, but continued to be somewhat irregular. Facial expression rapidly became normal. The patient was discharged cured on June 14, in normal health.

DISCUSSION.

The Clinical Picture. The picture given here is a composite one and is intended to show the majority of the clinical findings, all of which do not occur in any one given case.

The onset in the majority of cases is insidious. At times, however, the onset may be sudden, with rapid development of the symptoms, as in Case I, and a marked tendency to irritability and restlessness rather than an initial lethargy. The temperature is usually normal, with a normal pulse and respiration ratio. Rarely, though at times, a sore-throat is noticed, as in Case II; more commonly diplopia, headache, either frontal or occipital, with a marked feeling of sleepiness, is complained of. In early cases these symptoms tend to make one think of a beginning meningitis, typhoid or poliomyelitis, but there is usually no trouble in ruling these out either on clinical grounds or laboratory findings within a few days. By far the commonest and most predominating symptoms at the onset have been the persistent feeling of malaise and sleepiness, from which the disease has taken its name. The next most common subjective symptom in our experience has been the diplopia.

As the disease progresses it has been a fairly constant finding to have some cranial nerve involvement. The commonest abnormality in this respect is to be seen in the eyes. Irregularity of the pupils, with sluggish reaction to the light, was seen in 1 case, ptosis of one or both lids in 2 cases, nystagmus in 2 cases, diplopia in 2 cases, strabismus of one or both eyes in 2 cases; the fundi, however, never have shown pathologic changes in our experience. There is one sign that we found in 4 of our cases and which does not seem to be discussed much in the literature. That is the marked absence of all facial expression, an ironing out of the facial lines, which gives them an appearance that is nearly typical of the "mask face" of paralysis agitans. This sign is persistent throughout the course of the disease, but seems to disappear with the loss of the lethargy and a return to normal mental activity. The patient's absolute loss of interest in his environment is portrayed extremely well in the facial appearance that he presents to the examiner. From the above findings it would seem that the oculomotor, trochlear, abducens and facial nerves are the ones most frequently affected, and that apparently the olfactory, auditory and optic nerves are never involved. The remaining physical findings vary and seem inconstant. Exaggeration of the superficial abdominal reflexes was observed in 2 cases and was present to normal degree in the remaining 3 cases. Brudzinski's sign was obtained in 1 case. In Case IV we found marked myotatic irritability of the muscles of the abdomen, thorax and upper extremities, and there was also present continuous spasmodic contractions of the entire abdominal muscle group. This lateral twitching was constant and persistent in this case, but was not found in any of the other cases.

In considering the laboratory findings as a part of the clinical picture we find that they are practically of no assistance, except where we consider the spinal fluid. Here, however, the findings are fairly characteristic and often are the deciding factor in arriving

at a definite diagnosis. The spinal fluid was always clear and the pressure was not increased. The cell count, however, was above normal and varied from seven cells per cubic millimeter to eighty-one cells per cubic millimeter, and were practically 100 per cent. mononuclear leukocytes. The cell count seemed to return to normal as the disease diminished in intensity. Globulin was present in every case. The Wassermann reaction was negative in every case. Smears and cultures were consistently negative. The colloidal gold curve, however, proved to be of interest in several cases. In Case IV the curve was tabetic in type in the first spinal fluid. The curve done on the second spinal fluid, drawn off eleven days later, was, however, paretic in type. In Case V the curve was tabetic in type on three separate occasions and the fluid was obtained at intervals of two and five days respectively. In the remaining cases the colloidal gold curve was negative. It would seem that the gold curve findings are variable and not consistent. Thus in Case III[1] of the series of Barker, Cross and Irwin the curve was on one occasion a "combined paretic and meningitic curve" and on another occasion was "leutic in type." The finding of either a luetic or paretic type curve, however, in a patient whose spinal fluid Wassermann is negative and whose clinical symptoms point to encephalitis should be of significant value.

The clinical course is usually typical. The patient remains in a lethargic state for a variable length of time and then spontaneously begins to wake up and gradually return to normal mental activity. At this time the cranial nerve findings diminish in intensity and disappear and the spinal fluid findings return to normal. Sequelæ are rare. In only 1 case (Case I) did we observe any marked after-effect, and in this case the flaccid paraplegia with the loss of the memory of how to walk rapidly passed away. Recovery is the usual terminal result, but in Case IV the patient died. This was the only mortality.

Etiology. The etiology at present is obscure to the last degree. It has been noticed, however, that in the majority of cases there is a preceding history of influenza, as in Case I, II, and IV of our series. This finding is not always constant, however, and what significance it may have on the ultimate etiology no one seems able to say. The smears and cultures taken from the spinal fluid are consistently negative and the absence of temperature, leukocytosis and other signs of sepsis tend to discredit the idea of the condition being an acute infection. The supposition of a filtrable virus is speculation at the best.

Pathology. The pathologic findings are well summarized in the autopsy report of Case IV. The gross anatomic findings showed

[1] Encephalitis, Lewellys F. Barker, M.D., Ernest S. Cross, M.D., and Stewart S. Irwin, M.D., Baltimore, Md., AMERICAN JOURNAL OF THE MEDICAL SCIENCES, 1920, clix, 170.

no apparent cause of death, there being observed only a chronic nephritis, edema and congestion of the lungs and an old pulmonary scar. Microscopic examination of the brain, however, proved illuminating. Sections taken from the centrum ovale, the right thalamus and right caudate nucleus showed a distinct massive perivascular infiltration which varied greatly with different vessels. There were also observed many globules of hyaline light purple substance, sometimes scattered along a diseased vessel, and Dr. Rolfe Floyd suggested that they might be what is known as brain sand. The inflammatory cells ran strictly true to type, no polynuclears being seen. The sections taken from the cortex showed a cortical softening in one area, but were otherwise normal. The pathologic findings in this case correspond to those of other observers and show that the pathology is practically all of a microscopic nature.

SUMMARY OF SPINAL FLUID FINDINGS.

Character.	Cells.	Differential.	Smear.	Culture.	Wassermann.	Globulin.	Colloidal gold.
CASE I							
1. Normal pressure, clear	11	Lymphocytes, 100 per cent.; polynuclear, 0	No organisms	Sterile	Negative	+ (1 plus)	1.2.2.1.1.1.2.0.0.
CASE II							
1. Normal pressure, clear	81	Lymphocytes, 100 per cent.; polynuclear, 0	No organisms	Sterile	Negative	+ (1 plus)	0.0.0.1.1.2.1.0.0.
2. Normal pressure, clear	8	Lymphocytes, 100 per cent.; polynuclear, 0	No organisms	Sterile	Negative	+ (1 plus)	0.0.1.1.1.0.0.0.0.
CASE III							
1. Normal pressure, clear	43	Lymphocytes, 96 per cent.; polynuclear, 4 per cent.	No organisms	Sterile	Negative	+ (1 plus)	0.0.1.1.2.0.0.1.0.
2. Normal pressure, clear	40	Lymphocytes, 100 per cent.; polynuclear, 0	No organisms	Sterile	Negative	+ (1 plus)	0.0.1.1.1.0.0.0.0.
CASE IV							
1. Normal pressure, clear	7	Lymphocytes, 100 per cent.; polynuclear, 0	No organisms	Sterile	Negative	+ (1 plus)	1.2.2.4.4.4.3.3.0.
2. Normal pressure, clear	7	Lymphocytes, 100 per cent.; polynuclear, 0	No organisms	Sterile	Negative	+ (1 plus)	5.5.4.3.3.3.3.2.0.
CASE V							
1. Normal pressure, clear	43	Lymphocytes, 100 per cent.; polynuclear, 0	No organisms	Sterile	Negative	+ (1 plus)	1.1.3.3.3.2.1.0.0.
2. Normal pressure, clear	36	Lymphocytes, 100 per cent.; polynuclear, 0	No organisms	Sterile	Negative	+ (1 plus)	1.1.3.4.4.3.2.1.0.
3. Normal pressure, clear	19	Lymphocytes, 100 per cent.; polynuclear, 0	No organisms	Sterile	Negative	+ (1 plus)	0.1.1.3.3.3.2.1.0.

Conclusions. 1. Epidemic encephalitis in the majority of cases appears to be preceded by influenza.

2. The commonest clinical symptoms are the lethargy, the "mask face" and the diplopia.

3. The spinal fluid findings show an increase in the mononuclear leukocyte content, varying from normal to about one hundred cells

per cubic millimeter. The colloidal gold curve is variable, but in the presence of a negative spinal fluid Wassermann a tabetic or paretic gold curve in a patient with clinical symptoms of encephalitis should be of significance in the diagnosis.

4. The etiology is extremely obscure.

5. The pathology is characterized by perivascular infiltration of round cells in the nuclei of the bulb.

6. The majority of patients recover, but mortality does occur.

A REPORT OF AN EPIDEMIC WITH CERTAIN CASES PRESENTING THE PICTURE OF MENINGO-ENCEPHALITIS.

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Of lethargic encephalitis Achard[1] aptly says, "La maladie est polymorphe et acyclique." Clinically, epidemic encephalitis presents a most interesting group of syndromes which vary widely in their symptomatology. From time to time various forms of this disease have been added to the lethargic type, the first to be described. Syndromes resembling paralysis agitans, catalepsy, chorea, mania, bulbar palsy and other conditions are of such frequent occurrence that the name "epidemic encephalitis" has largely replaced the original term "lethargic encephalitis."

The lesions of this disease are fairly definitely limited to the brain-stem and the basal ganglia and consist of a perivascular infiltration of lymphocytes and plasma cells, engorgement of the vessels and degenerative changes in the ganglionic cells. The pathological changes, being most commonly confined to the brain-stem and basal ganglia, are sufficient to produce most, if not all, of the various syndromes described.

As a rule, however, the meninges have been relatively uninvolved by the pathologic process and examinations of the cerebrospinal fluid have seldom given a cell count that would indicate any marked degree of meningitis.

Hala and Smith[2] reported 1 case with definite signs of meningitis: The cell count in the cerebrospinal fluid was 480 cells per c.mm. and on the thirtieth day after the onset a motile, gram-negative bacillus

[1] Lethargic Encephalitis, Bull. de l'Acad. de méd., Paris, 1920, lxxxiii, 106.

[2] A Case of Meningo-encephalitis (Lethargic Encephalitis), Arch. Neurol. and Psych., 1920, iii, 160.

was found in smears from the spinal fluid. The pathological examination showed a purulent exudate in the sulci between the convolutions and a bacillus similar to the one in the spinal fluid was found present in the exudate. Laboratory animals died three to seven days after inoculation. The authors state that "the cultural characteristics of this organism on sugar coincide with those of no other organism which we know." Their conclusion is that "the bacillus probably belongs to some intermediate class of the colon-typhoid-enteritidis group."

Barker, Cross and Irwin[3] stated that "only in a relatively few cases are the clinical signs of an outspoken meningeal irritation present. In one of our series there was pain in the neck and back, some rigidity of the neck, a positive Brudzinski sign and a positive Kernig sign. That there is a slight patchy involvement of the leptomeninges in the inflammatory process in many cases has been shown, however, by postmortem examinations and by the increased cell count and the positive globulin reactions in the cerebrospinal fluid."

Tilney and Riley[4] found definite pathological changes in the spinal fluid in only 1 case out of 15. A diplostreptococcus was present in the fluid upon incubation, on culture, and in the stained smears. Subsequent tests of the fluid in the same case failed to show any organism to be present.

Bassoe and Hassin[5] noted in one of their cases pial changes indicative of a mild leptomeningitis. The pia-arachnoid was infiltrated and frequently showed distended meshes containing congested hyperemic vessels.

Flexner[6] reported increased cells and globulin in the cerebrospinal fluid but less than in poliomyelitis or meningitis.

Heiman[7] states that there is frequently moderate rigidity of the neck. Of eight spinal fluids examined he found definite changes in only one, which had a cell count of 80 and a positive albumin test.

Bassoe[8] suggests with some hesitation that this virus also may produce a syndrome characterized by meningeal irritation, and by irritation or paralysis referable to the spinal or cranial nerve roots. He reports 2 cases of this type.

[3] On the Epidemic of Acute and Subacute Non-suppurative Inflammations of the Nervous System Prevalent in the United States in 1918–1919; Encephalomyelitis; Polyneuritis and Meningo-encephalomyeloneuritis, Am. Jour. Med. Sc., 1920, clix, 170.

[4] Epidemic Encephalitis, Neurol. Bull., 1919, ii, 106.

[5] A Contribution to the Histopathology of Epidemic (Lethargic) Encephalitis, Arch. Neurol. and Psych., 1919, ii, 24.

[6] Histologic, Pathological and Clinical Facts and Epidemology in Brief, Jour. Am. Med. Assn., March 27, 1920, lxxiv, 865.

[7] Am. Ped. Soc. and Jour. Am. Med. Assn., July 19, 1919.

[8] The Delirious and Meningoradicular Type of Epidemic Encephalitis, Jour. Am. Med. Assn., 1920, lxxiv, 1009.

In a study of the literature with reference to the epidemiology of epidemic encephalitis, we found no reports of any definite contagiousness or of any tendency for the disease to spread through a household.

In the Local Government Board Report[9] it is noted that of 58 cases investigated there was no instance of more than 1 case in the same household and Draper in this report says there was but one instance of more than 1 case in a family.

The following series of cases is of special interest because of the marked meningeal symptoms, the high degree of multiple incidence, the change in type of involvement and course and the bacteriological findings.

The epidemic occurred in a village of 743 people in southwestern Minnesota. There were 11 cases: 5 of which were in two related families; of the other 6 there were 3 in one family and 2 in another family. Six of the 11 patients died. Two of these patients were seen by one of us during their illness. Case No. IX was seen two weeks after the onset and case No. X was examined one week after the onset of the disease.

Case I.—T. D., male, aged nineteen years, was the first possible case. He had not been in good health since 1916, when he was operated for exophthalmic goiter. His fellow workmen in the local produce company where he was employed had noticed an apparent failure in strength for several weeks before the onset of the acute symptoms.

On December 9, 1919, he came home from work complaining of not feeling well. The following morning he was nauseated and his chief symptom was fatigue. At 10.00 P.M., December 10, he became restless and delirious. A physician, who was called only shortly before death, noted some pulmonary involvement with blood tinged sputum and made a diagnosis of pneumonia. Death occurred at 3.00 A.M. December 11, about twenty-one hours after onset of symptoms.

Case II.—M. G., male, aged twenty-five years, came to the village December 9 and left for home at noon, December 12. While in the village, he lived with his brother (Case VII) and his brother's wife (Case IX). This brother was the local butcher with a shop next door to the produce company where T. D. (Case I) worked. M. G. became ill on his way home on the train during the night of December 12–13. On the morning of December 13, he was driven from the station to his farm, became unconscious soon after his arrival home and died December 14 at 9.00 P.M. The entire dura-

[9] Report of an Inquiry into an Obscure Disease, Encephalitis Lethargica, 1918. Reports of Local Government Board on Public Health and Medical Subjects, London, New Series No. 121.

tion of illness was about forty-eight hours. The diagnosis in this case was said to have been spotted fever.

CASE III.—J. R. (son of patient No. IV), male, aged ten years, became ill December 12 at 2.00 P.M. and died December 13 at 2.00 P.M. During his illness, he was not restless, but vomited a few hours after the onset of the illness and was delirious during the night. He did not seem to be in great pain or to suffer from distress. There was no Kernig or rigidity of the neck at any time.

CASE IV.—R. R. (mother of patient No. III), female, aged forty-one years, became ill December 13 with severe headache, mostly in the back of the head. The next morning, there was a purpuric rash on body and the temperature was 100.4° and the pulse 80. She got up, however, and walked about the room. On December 15 she complained of headache, backache, vomiting and pains in the limbs. At this time, she stated that she felt well except for the need of a good night's sleep. There was occasional deafness from the second day of illness. She felt drowsy most of the time but would answer questions rationally. There was a slight icteric tinge to the sclera. There was no Kernig or rigidity at any time. The leukocyte count of the blood was 34,300 per c.mm. Death occurred December 18 after a period of partial unconsciousness. The duration of the illness was about five days.

Autopsy was performed December 20, 1919, thirty-eight hours after death. The body was embalmed very shortly after death. The body was that of a well-developed stout woman. There was no edema; there was an icteric tinge to the scleræ of the eyes but this was not demonstrable on the skin. Small petechiæ were seen over the chest, abdomen, arms, hands and thighs. There were a few fresh fibrinous adhesions over the lateral and interlobar surfaces of the right lung. There was no pneumonia found. The spleen weighed 230 grams and showed the gross and microscopic evidences of acute splenitis. The liver showed fatty metamorphosis and chronic passive hyperemia. The kidneys showed moderate cloudy swelling both grossly and microscopically.

The brain showed a fairly large amount of greenish very thick purulent exudate in the pia-arachnoid over both cerebral hemispheres, especially in the sulci. This exudate was also found over the superior surface of the cerebellum. All the meningeal vessels were dilated, especially those on the left side. The lateral ventricles and the third ventricle contained no excess of fluid. Careful coronal sectioning of the brain showed no gross lesions in the brain substance. Smears of the meningeal exudate showed large numbers of polymorphonuclears and a moderate number of mononuclears leukocytes. There were a very few possible intracellular diplococci but one could not be absolutely certain about

these. No microscopic sections were made from the brain substance. The body had been embalmed so that cultural study was impossible.

CASE V.—H. K. (brother of patient No. VIII and nephew of patients Nos. VI and X and all lived in the same house), male, aged five years, became ill during the forenoon of December 18. He began to lie around during the afternoon but did not want to go to bed. In the evening when the father returned from work he noticed the boy looked very ill and called a physician, who made a diagnosis of epidemic cerebrospinal meningitis and gave 15 c.c. of serum intraspinously. Patient did not complain of pain, and fever was not observed until shortly before death. There was a petechial rash scattered over the body. A spinal fluid examination from a puncture done on the evening of the 18th showed a very slightly cloudy fluid. The Nonne and cell count were negative and no organisms were found in smears or cultures (the spinal fluid examinations in these cases were made forty-eight to sixty hours after the spinal puncture, having been sent through the mail to Minneapolis). The patient died at 10.00 A.M., December 19, after an illness of only twenty-four hours.

Autopsy was performed December 20, 1919, twenty-nine hours after death. The body was that of a well-developed and well-nourished boy. There was no edema or jaundice. Scattered hemorrhages varying from the size of a pinhead to a diameter of 3 cm. were present in the skin of the trunk, limbs and face. Examination was permitted for the head only.

The meninges over the convex surface of the cerebrum showed moderate edema with a small amount of thick greenish purulent exudate in some of the sulci. There was a small amount of glairy semisolid material (not purulent) in the posterior horns of the lateral ventricles. Careful coronal sectioning of the brain showed no gross lesions within the brain substance. Smears of the meningeal exudate showed a predominance of polymorphonuclear leukocytes. Some cells showed what suggested intracellular gram-negative diplococci but in no instance were the organisms absolutely definitely demonstrated. Cultures from the meninges and lateral ventricles remained sterile.

Sections of the cortex extending for over 1 cm. into the cerebrum showed microscopically congestion of the vessels with perivascular lymphocytic infiltration. There was a proliferation of glial tissue and a diffuse lymphocytic infiltration. The neurone cells showed chromatolysis with invasion of lymphocytes (satellitosis and neuronophagia). These changes were found in the parts of the sections farthest from the surface of the brain.

The autopsies on this and the previous case were done on the same day. At that time it seemed probable to the pathologist

that he was dealing with cases of epidemic cerebrospinal meningitis; the first case had shown an abundant greenish thick purulent meningeal exudate with no sign of gross lesions in the brain substance. The smaller amount of the purulent meningeal exudate in the second case was thought to be due to the shorter duration of the illness with death presumably in the stage of general bacteremia and just as the infection was beginning to localize in the meninges. Examinations of smears from the meningeal exudate were quite suggestive also. The encephalitis was proved only when the microscopic sections were examined. The lymphocytic character of the perivascular and diffuse infiltration; the depth to which the affection extended; the degree of the neuron cell changes all serve to differentiate this encephalitis from the shallow hemorrhagic encephalitis with polymorphonuclear leukocytic infiltration sometimes associated with the meningococcic meningitis.

CASE VI.—R. D. (sister of patient No. X and aunt of patients Nos. V and VIII and living with them), female, aged nine years, came home December 18 with stomachache and sat about the house during the day without expressing desires or complaining. Later there was headache, vomiting and general irritability. Serum treatment was started and continued through the illness. There was a positive Kernig the following day and the purpuric spots and herpes were present. Vision was lost in one eye on the 24th. Rigidity was noted as being less and hearing not so acute on December 25. Parotitis developed on the 29th. The attending physician considered the possibility of the condition being lethargic encephalitis. During the latter part of her illness she slept most of the time but her mind was clear when awake. The temperature went as high as 102° to 103° until January 2. Two spinal fluid examinations were made. December 20 the fluid was clear, Nonne and cell count negative and no organisms were present in smears or cultures. December 25: clear fluid, Nonne trace, cell count negative, no organisms in smears or cultures.

CASE VII.—J. G., male, aged twenty-nine years, living with patients Nos. II and IX and working next door to patient No. I, complained of general weakness on December 19. He had headaches, bowel disturbances and pain in the abdomen. No Kernig or rigidity was noted. He returned to work the following day and was considered as a possible abortive case.

CASE VIII.—M. K., female, aged thirteen years, living with patients Nos. V, VI and X, became ill about 11.00 A.M., December 21. On that date she complained of a mild headache and some pain in the back. The temperature was 102.5° and the pulse 120. She had a tendency to a positive Kernig and there was some pain

upon bending the neck. By the 24th she was apparently well. Spinal fluid examination on the 22d showed a clear fluid with a negative Nonne and normal cell count. No organisms were found in smears or cultures.

Case IX.—C. G., female, aged twenty-five years, living with patients Nos. II and VII, began to have headache and vomited on December 24. There was some muscular rigidity after the third day and the Kernig sign was positive early in the course of the disease. Deafness developed on the 25th and blindness in the left eye on the 26th. There was general hyperesthesia from the onset of the illness. An erythematous eruption appeared on the 27th. She would talk rationally when someone was conversing with her but otherwise talked more or less irrationally. Headache was severe and persistent from the first. Hearing gradually returned and when last seen on January 11th, the patient was apparently slowly recovering. A spinal fluid examination made December 27th showed a slightly cloudy blood tinged fluid with a normal cell count and no organisms present in the smears. A Gram-positive organism was found in the broth cultures, but there was no growth on serum. On December 28 the fluid was cloudy, pus cells were present and staphylococci were found in smears and in broth and serum. The fluid examination on the 29th gave a cloudy fluid, flocculent. Pus cells were present but no organisms were found in smears or cultures.

Case X.—R. D., male, aged twelve years, became ill on December 30. At the time of onset he was living with patients Nos. V, VI and VIII. His past history was negative except that he had had anterior poliomyelitis in 1916. His illness began with restlessness and pain in the distribution of the left supra-orbital nerve. On the 31st he complained of tenderness over the left eye. There was no rigidity or tremor. The pulse was 78 and the temperature 98.4°. On the second day of his illness there developed deep and rapid respiration with a respiratory rate of 40 to 60 a minute. There was occasional vomiting. The blood examination at this time showed a leukocyte blood count of 17,000. On January 1 he was able to walk to an automobile, go to another house nine miles away from the village, and walk upstairs to bed. The blood examination on January 4 gave a leukocyte count of 7600 and a red blood cell count of 4,000,000. On this date, there was some cough and expectoration, and percussion gave a higher pitched note over the right upper lobe. Temperature was 101° and the pulse 90. He became semidelirious on the 5th. He answered questions readily and there was no difficulty in his understanding what was said to him. His condition became worse on the seventh but there was no Kernig present and only slight rigidity on extreme

flexion of the neck. In the following few days the mild delirium continued. He would pick at imaginary objects in the air but

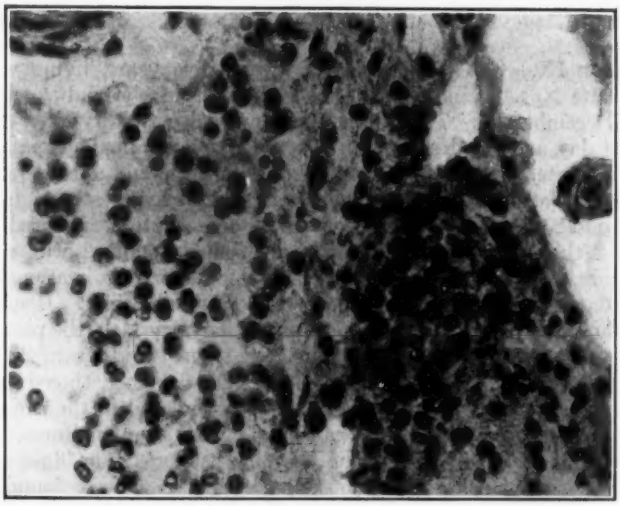

FIG. 1.—Case X. Meninges over cerebral cortex. Arachnoid infiltrated with polymorphonuclears, lymphocytes and endothelial leukocytes. Some extravascular red blood cells also shown.

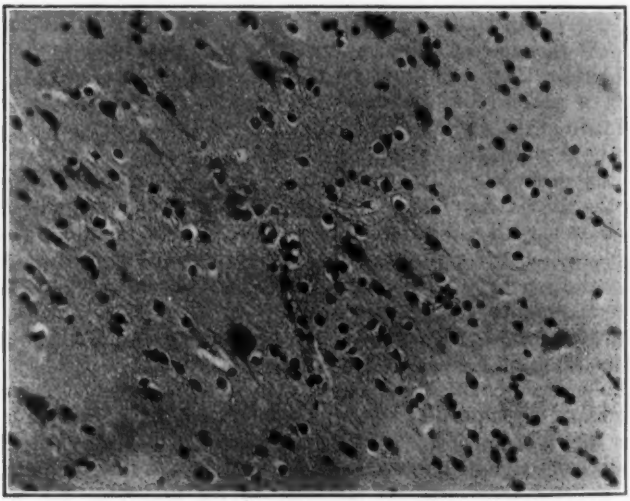

FIG. 2.—Case X. Subcortical white matter of cerebrum. Diffuse lymphocytic infiltration and glial proliferation.

memory and comprehension were unimpaired and in conversation he appeared normal. A neurological examination made on January 9 gave the following findings: Vision was subjectively fair; he saw objects larger or smaller at times. The fundi were normal

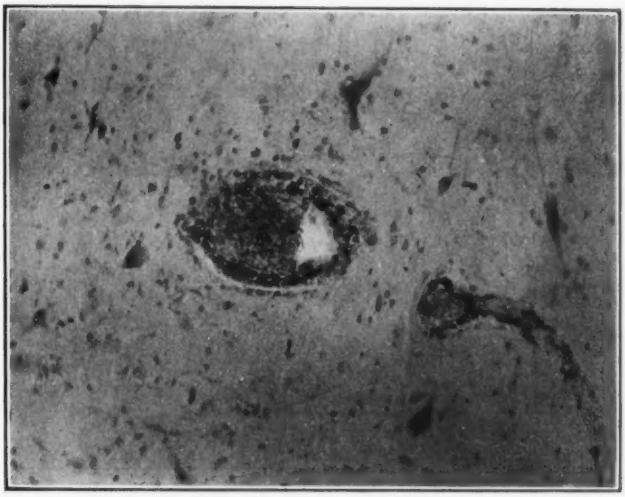

FIG. 3.—Case X. Midbrain. Perivascular lymphocytic infiltration.

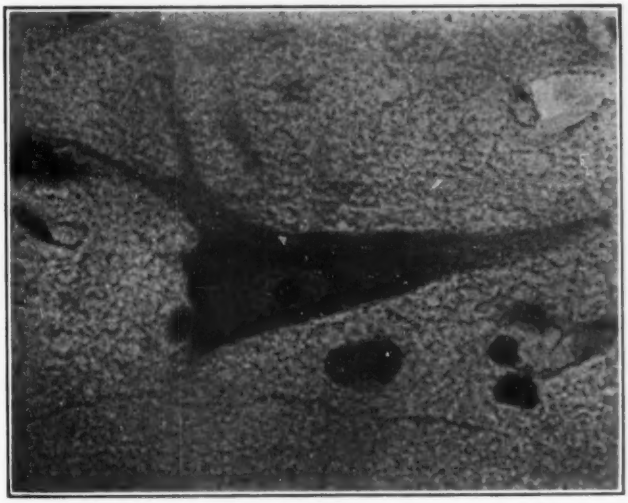

FIG. 4.—Case X. Region of cortex. Satellitosis and chromatolysis of neurone cell.

except for a very slight edema of the disks. There was weakness of the right lateral rectus and a slight ptosis. The pupils were unequal but reacted normally to light and distance. There was

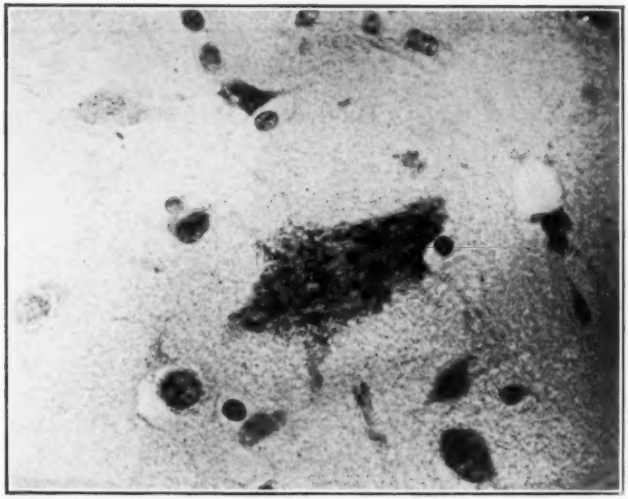

FIG. 5.—Case X. Region of cortex. Disintegration of neurone cell; also shows neuronophagia beginning.

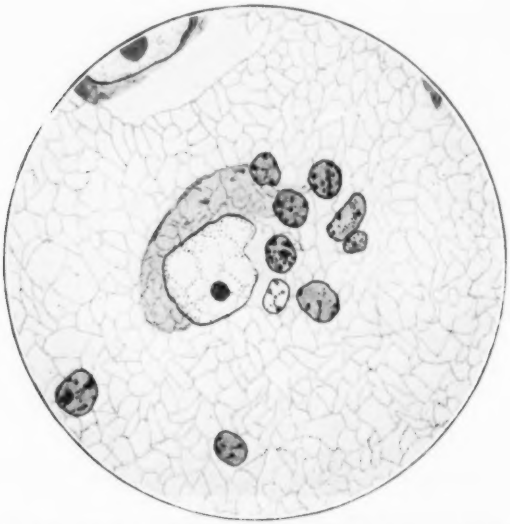

FIG. 6.—Case X. Basal ganglia. Advanced neuronophagia.

no diplopia; convergence was good. On looking to the right a very marked nystagmus was present. A twitching of the facial muscles was noted. Hearing was normal. Swallowing was unimpaired. The relatives thought that there was some change in his voice. He did not ordinarily complain of pain, but his sister said he complained of pain when bathed and of pain at times in the knees. Pressure over the extremities or stroking did not cause discomfort.

There was no atrophy present except in the left leg (poliomyelitis in 1916). General motor and psychic restlessness was evident. He constantly tossed about and had a coarse jerking of the arms and legs. In a general way this resembled choreic restlessness,

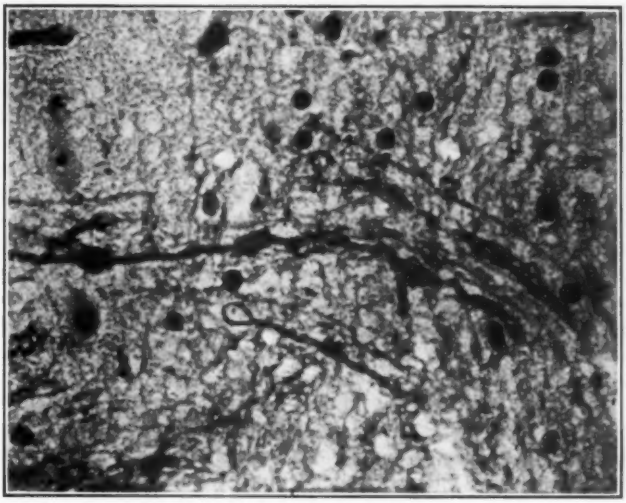

FIG. 7.—Case X. Internal capsule in region of thalamus. Myelin sheath degeneration; showing bulbous enlargements and irregular thickening of the sheaths.

but the movements were coarser and more purposeful although involuntary. A degree of ataxia was noted in the movements of the hands. The deep reflexes were all moderately active except in the left leg where the knee-jerk was absent and the ankle-jerk was much diminished. The plantar reflexes were both flexor in type and there was no ankle clonus. The abdominal reflexes were present. Memory and comprehension were good. He answered questions readily and intelligently. When not in conversation he sang and hummed to himself and also muttered some. He complained of feeling tired and drowsy and went to sleep at times while eating. Spinal fluid examination made January 8 showed a clear fluid, Nonne negative, normal cell count and no organisms

in the smears. Gram-positive staphylococci were present in the cultures. He died January 23, 1920, forty-one days after the onset of his illness.

At autopsy, January 25, 1920; thirty-three hours postmortem, the body was well developed and well nourished. There was no edema or jaundice and the pupils were regular and equal. The lips showed sordes. The serous cavities showed no adhesions and no excess fluid. On the anterior surface of the heart in the epicardium were about a dozen petechial hemorrhages, especially over the right ventricle. There were no other gross lesions in the heart aside from a slight hypertrophy of the left ventricles. The lungs showed no lesions aside from edema in the lower lobes. The spleen was enlarged and very soft and flabby. It showed acute splenitis both grossly and microscopically. The kidneys showed cloudy swelling. On the outer surface of the skull there were a few small hemorrhages. The upper surface of the cerebrum showed a considerable collection of serous fluid which was very slightly cloudy. On the inferior surface of the frontal and parietal lobes and over all the surface of the cerebellum, midbrain, pons, medulla and cervical portion of spinal cord there was congestion of the meningeal vessels with many small hemorrhages. Over these same areas there was a thick fibrinous exudate and in the sylvian fissure this exudate was fibrinopurulent in spots, causing obliteration of the fissure by adhesion. There was about 2.5 c.c. of clear fluid in each lateral ventricle. There was a small amount of thin serous exudate in both middle ears and mastoid cells. The mucous membranes of the middle ears were thickened. The frontal, ethmoid and sphenoid sinuses were normal.

On microscopic examination the various gross findings in the organs of the thorax and abdomen were corroborated. The brain, however, showed significant lesions. In the meninges there was a marked exudate in the subarachnoid space in addition to the edema and hemorrhages noted grossly. In the exudate medium-sized mononuclear leukocytes predominated. There were also numerous polymorphonuclear leukocytes and some lymphocytes. Brain substance: there was a perivascular lymphocytic infiltration, especially marked in the region of the basal nuclei and red nucleus, and somewhat in the cerebellum. Satellitosis, neuronophagia, chromatolysis and further neurone cell degenerations were found especially in the basal nuclei and pons. There was a very marked irregular swelling of the medullary nerve sheaths in the midbrain and pons with irregular thickenings of these sheaths. Small amounts of brown pigment were noted in some cells in the pons not far below the locus cæruleus. At least one clump of small bacilli was found in a stained section of the pons but no further bacteria could be demonstrated even in sections stained for both Gram-negative and

Gram-positive organisms. Cultures from the meninges, ventricles and brain substances were sterile.

Small bits of brain tissue removed from cortex, midbrain and pons, under aseptic precautions, were taken to the Division of Preventable Diseases of the State Board of Health and there inoculated intradurally into rabbits.

One rabbit died approximately forty-eight hours after inoculation. The other rabbits remained alive and apparently well. At autopsy the rabbit which died showed a very heavy fibrinous exudate over the lower lobe of the right lung and congestion of the organs, but no other gross lesions. A very small Gram-negative bacillus growing well on ordinary media was demonstrated in both pleura and heart's blood. This condition may possibly, though not necessarily, have been present before the inoculation. The microscopic examination of the brain was nevertheless significant and it seems entirely possible that the condition found there was related to the inoculation rather than to the pleuritis and bacteremia. In the meninges there was congestion with slight hemorrhage and rather slight diffuse exudate consisting principally of lymphocytes and plasma cells. The midbrain showed a marked perivascular infiltration of lymphocytes and diffuse lymphocytic infiltration and various degrees of degeneration of the large nerve cells with chromatolysis, satellitosis and neuronophagia. Perivascular lymphocytic infiltration was found also in the cerebrum and pons.

Case XI.—After our last visit to the village, another case has developed in the family (X) and within six days after his death, and, therefore, related to patients Nos. VI, VII, VIII and X. This patient, T. K., aged fifteen years, is said to have had a typical lethargic type of encephalitis. The first symptom was noted January 29, 1920.

Discussion. In these cases we have a rather remarkable sequence. The first cases (I, II and III) presented more or less the picture of an acute toxic condition without special localizing phenomena. In the next group (IV, V, VI, VIII and IX) the meningeal symptoms were prominent with, however, fairly definite evidence of an accompanying encephalitis. The last two cases (X and XI) were primarily encephalitis, with meningeal involvement occurring seven days after the onset of the symptoms in case No. X. In other words there was an infection of an extremely virulent type gradually becoming attenuated and presenting in this course three fairly distinct syndromes—an acute toxemia, a meningitis or meningo-encephalitis and an encephalitis.

In this connection it is interesting to note that in some of the previous epidemics botulism was suspected and a number of cases so diagnosed according to the report of the Local Government

Board (London). In the first cases of our series, botulism was thought of as a not unlikely diagnosis. The infection in these cases was so virulent and the course so acute that few localizing phenomena were present.

It seems likely that these cases are related etiologically to the hitherto reported cases of epidemic encephalitis. Two of these cases presented typical syndromes of "lethargic encephalitis," one of these (No. X) having the choreiform movements seen in a certain number of cases of epidemic encephalitis as well as the characteristic lethargy. In the history of case No. IV we note that the patient stated that she felt well except for the need of a good night's sleep. She was drowsy most of the time but would answer questions rationally.

The autopsies of cases Nos. V and X show lesions typical of epidemic encephalitis.

The perivascular lymphocytic infiltration, most marked in the region of the basal nuclei, the diffuse lymphocytic infiltration with glial proliferation, the degenerative changes in the nerve cells, the satellitosis and neuronophagia, have all been repeatedly described time and again in reports of epidemic encephalitis. The fact that these lesions may be found in the brain cortex, as in our case No. V, has previously been demonstrated in Bassoe's series of cases.

Pathologically, the distinctive feature in this series of cases is the extraordinary prominence of the meningitis. Although meningeal affection has been described by Bassoe and Hala and Smith we have seen no reports of cases showing such an extensive and marked involvement.

The acuteness of the disease process and the mortality of this epidemic are unusual. The mortality was 54.5 per cent. even when case No. VII is included (abortive case). Three of the 6 fatal cases died within approximately twenty-four hours of onset and one other died within forty-eight hours; one after five days and one after forty-one days. Epidemic encephalitis has hitherto been considered generally as a less acute disease with a fairly low mortality.

Besides the acuteness of the disease process and the marked meningeal involvement, these cases are notable for apparent contagiousness. There is a definite relationship between cases Nos. I, II, VII and IX; patients Nos. II, VII and IX lived in one house; patient No. I worked next door to patient No. VII. Patients Nos. III and IV lived in one house and became ill at almost the same time. Patients Nos. V, VI, VIII and X became ill while in the same house and within a period of eight days. During his illness patient No. X was taken to another house; within a short time after his death and in the house where he died, case XI developed the disease. All the 11 cases are included in these three

groups. The first 10 of the 11 cases developed within a period of thirteen days.

	Duration.	Outcome.	Date of onset.	Relationship.
I . . .	21 hours	Died	Dec. 9, 1919	a
II . . .	48 hours	"	Dec. 12, 1919	a
III . . .	24 hours	"	Dec. 12, 1919	b
IV . . .	5 days	"	Dec. 13, 1919	b
V . . .	24 hours	"	Dec. 18, 1919	c
VI . . .	7 days	Lived	Dec. 18, 1919	c
VII . . .	1 day	"	Dec. 19, 1919	a
VIII . . .	3 days	"	Dec. 21, 1919	c
IX . . .	?	"	Dec. 24, 1919	a
X . . .	41 days	Died	Dec. 30, 1919	c
XI . . .	?	?	Jan. 23, 1920	c

Summary. This paper contains a report of 11 cases divided into three groups according to the symptomatology. The first group presented the syndrome of an acute toxic condition; the second group that of a meningitis or meningo-encephalitis and the third group the clinical and pathological findings of epidemic encephalitis. In these cases there was a definite diminution of acuteness in the latter cases and there was an evident contagiousness present in the whole group of cases.

Note. We wish to express our appreciation to Doctors Metcalf, McCrae and Stanley of Fulda, Minnesota, for the courtesy of allowing us to use their clinical records of these cases; to the members of the Division of Communicable Diseases of the State Board of Health for their kindness in making these cases available to us and for the use of their bacteriological and serological records; to Doctors H. E. Robertson and A. S. Hamilton, Chiefs of the Department of Pathology and Public Health and the Division of Nervous and Mental Disease respectively, to Dr. J. C. McKinley for the drawing and to Mr. Henry Morris for the microphotographs.

ANEURYSM OF THE HEPATIC ARTERY: WITH THE REPORT OF A CASE.*

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Aneurysm of the hepatic artery is a very rare condition, only 54 cases appearing in literature. In 1908, Rolland[1] published a study of 40 cases and at the same time reported a case of his own. In addition the following cases have been recorded and are given in

* Reported by Dr. Thomas McCrae with special reference to the clinical features in the International Clinics for September, 1920.

[1] Glasgow Med. Jour., 1908, lxix, 342–358.

the order of their publication: Schupfer,[2] Bickhardt[3] (2 cases), Reichman,[4] Tuffier,[5] Dean and Falconer,[6] Friedman,[7] Merkel,[8] Fleckenstein,[9] Baruch,[10] Teacher and Jack,[11] Anderson,[12] and Kading.[13]

No review of recorded cases could be found in American literature.

The condition is interesting also from the viewpoint of its etiology; syphilis does not play the same important part as in aneurysm in general.

Case Report.

The patient, a white male aged fifty years, a plumber, was admitted to the Jefferson Hospital in the service of Dr. Thomas McCrae on March 1, 1920.

Family History. There is nothing of particular importance in regard to his parents, brothers and sisters. He has been married twice. By the first marriage there were four children, all of whom died at the age of three years, five years, two months, and one month but no accurate account of the cause of death can be obtained. His second wife had one pregnancy, which resulted in a miscarriage.

Personal History. The patient as a rule has been very healthy. The only acute illness which he had was paratyphoid fever eight years ago, from which he made a good recovery. As he was in a hospital with this illness and his case was carefully studied the diagnosis is probably correct. He states that comment was made on the diagnosis of paratyphoid fever. Five years ago he had a sharp severe pain in the epigastrium lasting about twenty-four hours. He does not remember much of the details, but is positive that there was no vomiting, and no jaundice following this attack. He has always had some trouble with constipation. There is no history of urinary disease and he denies gonorrhea and syphilis. He has used alcohol very moderately. He has always regarded himself as being an exceptionally strong man. There has not been any change in weight. His occupation is entirely executive and he does not handle lead in any form.

Present Illness. On the day of onset the patient states that he arose at his usual hour feeling perfectly well, took his ordinary very simple breakfast and had been attending to his business all morning.

[2] Gazz. d. Osp., August 26, 1906.
[3] Deutsch. Arch. f. klin. Med., Leipzig, 1907, xc, 289–309.
[4] Virchows Arch., 1908, cxciv, 71–114.
[5] Presse méd., Paris, 1909, xvii, 153.
[6] Edinburgh Med. Jour., 1912, n. s., viii, 124–131.
[7] Med. Rec., 1912, lxxxii, 522–525.
[8] Virchows Arch., 1913, ccxiv, 289–301.
[9] Inaug. Diss., Giessen, 1913.
[10] Beiträg. z. klin. Chir., Tübingen, 1915, xcv, 502–512.
[11] Glasgow Med. Jour., 1916, lxxxvi, 277–285.
[12] Tennessee State Med. Assn. Jour., December, 1919, xii, 286.
[13] Deutsch. Ztschr. f. Chir., Leipzig, cl, 1–2, 82.

About 1 P.M., while standing on the street talking to a friend, he felt a sudden burning sensation which he indicates as situated in the center of the abdomen occupying a circular space about six inches in diameter with the navel as a center. Almost immediately after this there was intense abdominal pain which he states was in the epigastrium. He thought that he was dying, had difficulty in standing, and broke into a very profuse sweat. He was only a short distance from the office of a friend and with assistance was able to reach it. His serious condition was recognized and the hospital ambulance was sent for at once.

Examination. The patient is very well nourished and has a high color. He is very seriously ill and suffering intense abdominal pain which causes him to writhe about in bed. There is a question as to whether the sclerotics show jaundice and it is best described as icteroid. Examination of the head and mouth is otherwise negative. The lungs are clear. The heart shows a very feeble impulse and no evidence of cardiac enlargement is found. The sounds are distant and feeble; the pulse is 66 and rather small but quite regular. The abdomen is somewhat distended. The patient points to the epigastric and umbilical regions as the seat of the pain. The abdominal walls are soft and do not show any rigidity even in the epigastrium. There is very slight abdominal tenderness on palpation which seems most marked about the navel. The contrast between the severe pain and the absence of rigidity and any marked tenderness is striking. No mass can be felt, and despite the distention it is possible to palpate satisfactorily. The sounds of peristalsis are well heard. When pressure is made over the lower costal region on the right side the patient states that he feels more comfortable. The leukocytes were 13,400.

At the time of admission the condition was very serious, the extremities were cold and he complained of numbness in the hands and feet. Soon after admission he began to vomit. There was no blood in the vomitus but a considerable quantity of bile. Not long after this there was a free movement of the bowels.

The condition improved in the following twenty-four hours and remained much the same during the whole course of the disease. The pain continued at intervals and required small doses of morphin to control it. There was constant fever, which varied, usually being 100° to 102°; the pulse-rate showed slight variation. The jaundice became very definite and rather deepened as the days went on. The leukocytes varied from 13,000 to 17,000; the Wassermann reaction was negative. The stools were negative and showed no evidence of disturbance of fat digestion or the presence of blood. The abdominal pain continued, became more localized in the upper epigastrium and below the right costal margin in the region of the gall-bladder. There was a considerable degree of tenderness in the region of the gall-bladder which gradually increased. As the

patient's condition was not improved, and the signs of local disease in the upper abdomen became more marked, with deepening of the jaundice, exploration seemed advisable. The most probable diagnosis was cholecystitis but it was felt that the picture was not quite the usual one of that disease and that some other condition might be found.

On March 9 at 1 P.M. the patient was carefully examined. There was no abdominal distention and the percussion note in the flanks was resonant. The patient's condition remained the same and at 4 P.M. the anesthetic was begun. After a few breaths the patient died suddenly. No change in his general appearance had been noted. The pulse at the time of beginning the anesthetic was 78.

Autopsy (performed twenty hours after death).

The body is that of an adult white male 70 inches in length, approximate weight 160 pounds. The pupils are moderately dilated and equal. The nostrils are negative. The teeth are in fair condition. The chest is full, the abdomen distended. The external genitals are apparently normal. There is no edema of the limbs. Postmortem rigidity is marked.

The peritoneal cavity contains a blood clot weighing 1600 gms., and considerable free blood. The intestines are constricted in several areas. Liver extends to costal margin in right midclavicular line. Gall-bladder is large and distended. Diaphragm extends to fourth rib on right, and to fourth interspace on left.

Pericardium contains a small quantity of clear serous fluid.

Heart weighs 375 gms. The muscle cuts with increased resistance and is pale red in color. Aortic cusps slightly thickened and stiffened. Mitral, pulmonic and tricuspid valves apparently normal. First portion of aorta contains several light yellow, sharply outlined areas of degeneration. Considerable sclerosis in anterior coronary artery.

Pleura and lungs apparently normal.

Spleen weighs 200 gms. Capsule is grayish. Organ fairly firm and cuts with normal resistance. Trabeculæ distinct.

Left adrenal weighs 20 gms., no macroscopic evidence of disease.

Left kidney weighs 190 gms. Organ is large and firm. Capsule strips readily, leaving a smooth surface. At upper pole is a firm, pale red area of infarction measuring 4 cm. in width at base, and extending 3 cm. into kidney substance. Cortex measures 1 cm. in width.

Right adrenal weighs 22 gms. No gross lesion observed.

Right kidney weighs 210 gms., is large and firm, and cuts with increased resistance. Section shows a large, reddish infarct in upper pole, and an anemic infarct in lower pole, each measuring 3 cm. at base (capsule) and 3 cm. in depth. Surface of kidney over the

infarct is raised and dark red. A thrombosed vein is seen at base of red infarct.

Ureters single and patulous. Bladder large and distended with amber color urine. No evidence of inflammation of mucosa.

Duodenum contains yellowish-green material. Ampulla of Vater is patulous; pressure on gall-bladder causes black viscid bile to exude from the common duct.

Pancreatic and bile ducts patulous.

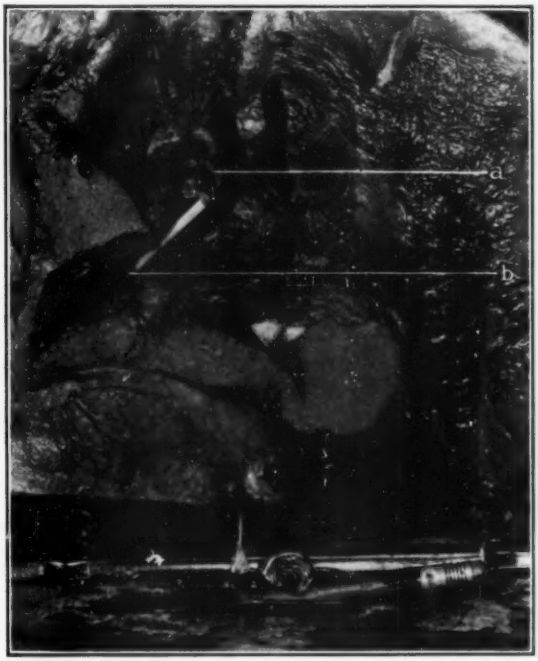

FIG. 1.—Inferior aspect of liver. *a*, aneurysm of hepatic artery; *b*, rod extending from aneurysm along tortuous branch filled with blood clot into liver substance.

Stomach small, thick-walled, rugæ obscured. No evidence of inflammation, ulceration or new growth.

Pancreas weighs 250 gms. Considerable clotted blood about head of organ. Tissue cuts with normal resistance. No gross evidence of disease.

Liver weighs 1680 gms., is large and firm. Surface mottled and smooth; outline regular. Cut surface is mottled and brownish-red. Gall-bladder is distended with black, viscid bile.

Lesser omentum is infiltrated with blood. Dissection shows the hepatic artery at its point of division into right and left terminal

branches to be sclerosed, and dilated into an egg-shaped mass measuring 2 cm. by 3 cm. The wall of this aneurysm has ruptured and its interior is partially filled with blood clot which extends by means of the branches into the liver substance. This rupture into the greater peritoneal cavity is apparently the site of the abdominal hemorrhage.

Aorta. Part of thoracic aorta comprises a cylindric mass 16 cm. in length extending along left side of vessel. On section it is found

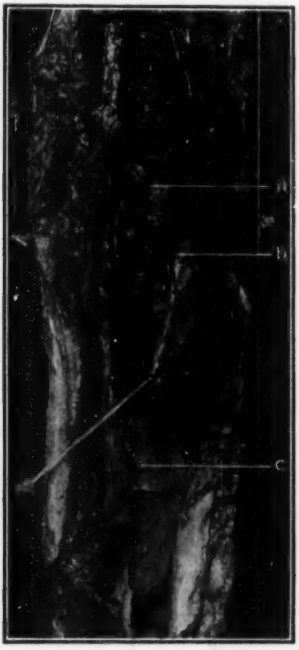

FIG. 2.—Outer surface of thoracic aorta from same case, showing dissecting aneurysm. *a*, blood clot lying between *b*, adventitial coat of vessel, and *c*, medial coat.

to be filled with clotted blood, occupying a position between the medial and adventitial coats of the vessel. No opening from the inner side of the vessel can be discovered. The inner surface of the aorta shows several crinkly yellowish nodular areas of degeneration, and many light yellowish striæ. The beginning of the left internal iliac artery is the seat of a fusiform aneurysm measuring 7 cm. in length and 4 cm. in diameter.

Microscopic Diagnosis: Marked congestion and edema of lungs; slight degree chronic interstitial splenitis; marked parenchymatous

degeneration of adrenal; slight hyperplasia of interstitial tissue. Kidney; tubular epithelium is in an advanced state of granular degeneration; that of the convoluted tubules is especially so and in addition swollen and desquamating. Considerable focal and diffuse hemorrhage both into tufts and tubules and interstitial tissue. Supportive structure is definitely increased, and in areas amounts to a patchy fibrosis; here and there are focal collections of small mononuclear cells in the interstitial tissue; "chronic diffuse

FIG. 3.—Inner surface of aorta, showing *a*, *a*, *a*, wrinkled patches of syphilitic aortitis.

nephritis." Granular degeneration of pancreas; chronic interstitial inflammation.

Liver: parenchymatous degeneration, passive congestion. Scattered throughout the liver substance and situated especially about the smaller vessels are focal collections of small mononuclear cells. Tangential section of one of the larger vessels shows its partial occlusion by an extending blood-clot. Many of the smaller bloodvessels show an extreme degree of obliterative endarteritis. The walls of the biliary ducts also show thickening and sclerosis, and in areas shedding of the epithelium.

Remarks. The presence of three aneurysms and the rather typical aortitis, together with the microscopic findings of perivascular collections of mononuclear cells, and the well-marked obliterative endarteritis affecting the smaller vessels of the liver, suggest that the process is syphilitic in spite of the fact that sections of the aorta stained by the Levaditi method failed to reveal the spirochete.

A study of the cases in the literature brings out the following points:

Etiology. Aneurysm of the hepatic artery is unique in that a majority of the cases have followed acute infectious processes, especially lobar pneumonia, rather than syphilis. In 26 cases in which the causative factor has been determined with some degree of certainty, aneurysm of the hepatic artery has followed such infections as pneumonia, osteomyelitis and typhoid fever, in 15 cases; syphilis in 5; atheromatous arteritis in 2; cholelithiasis in 2; trauma in 1, and tuberculosis in 1.

Rolland believes that gall-stones may be responsible for the aneurysm by direct injury of the arterial wall, and considers infective emboli as the probable cause in cases following infections. Schupfer reports a case following croupous pneumonia and concludes that the aneurysm resulted from acute infectious arteritis which was produced by the infective agents carried through the vasa vasorum. Grunert[14] considers that 73 per cent. of the 34 cases collected by himself were sequelæ of previous infectious processes.

Rolland believes that syphilis is an important factor and mentions it as directly responsible in the cases reported by Sacquipie[15] and Watzold.[16] In describing the changes observed in his case Watzold states that "the arteries show a definite thickening of intima and adventitia; the latter consists mostly of a broad circle of very cellular connective tissue. Almost all vessels show a considerable thickening of the intima which in many instances has resulted almost, or quite, in obliteration." In Rolland's own case changes in the arteries were noted as in the foregoing, and in addition hyalin degeneration of the vessel walls. The case reported by Teacher and Jack showed a widespread patchy subacute inflammatory condition of the hepatic arteries, which has been described as periarteritis nodosa. They state that the cause of this condition is not clear but there is evidence of its syphilitic origin. In addition, the arch of the aorta was thickened and irregular and all solid organs showed a very striking old endarteritis obliterans affecting the smaller vessels, principally those less than 2 mm. in diameter. The cases cited prove that the branches of the hepatic artery may be the seat of a definite panarteritis, as is true in the case under consideration. This condition is undoubtedly a cause of hepatic aneurysm.

[14] Deutsch. Ztschr. f. Chir., lxxi, 158.
[15] Zentralbl. f. path. Anat., 1900, xi, 748.
[16] München. med. Wchnschr., liii, 2107.

Baruch, in his excellent review, states that lues does not seem to be an important factor but that the condition usually follows previous infectious disease, especially pneumonia. The pneumonia usually involves the right side, and Baruch quotes Stumph as stating that in such cases edema of the periportal connective tissue was observed. If there is any connection between this inflammatory process and aneurysm formation it has not been established.

Ross and Osler[17] reported a case in which the patient died with symptoms of pyemia and the liver was found on section to contain multiple abscesses.

Concerning the *age* incidence, Tuffier and Villandre in a collection of 41 cases conclude that the condition is most common in youth. Rolland's review mentions cases from fourteen to eighty-three years, the average age being thirty-seven. Of 39 cases, 30 occurred in men and 9 in women. The average age of 8 female cases was forty-five years; of 28 males cases thirty-five years. Occupation apparently played no part.

Pathology. Rolland divides his cases into extra- and intrahepatic, the majority belonging to the former classification. In his collection 24 were extrahepatic and 8 intrahepatic; and in 2 cases, in each of which 2 aneurysms existed, one was extrahepatic and one intrahepatic. The main trunk of the artery has been affected more often than either of its branches. In 16 cases the main vessel was involved, in 12 the aneurysm was on the right branch and in 3 on the left. In 3 cases an aneurysm was found on each of the branches. In one case an aneurysm involved the cystic artery. In 6 cases the aneurysm was intact; in 32 the sac was ruptured. Rupture occurs in the majority of cases either into the peritoneal cavity or into the bile passages. In 16 cases rupture occurred into the peritoneal cavity, in 13 into the bile passages and in 3 into the stomach, duodenum or portal vein. The aneurysm may undergo spontaneous healing. In one case (Ledieu[18]) the aneurysm was occluded by a thrombus, the patient dying of renal disease with no symptoms referable to the liver. Extrahepatic aneurysms are generally larger than intrahepatic. The average size is that of a hen's egg—in one case it was the size of a child's head (Wallmann[19]). Sacquipie was the first to point out the importance of aneurysm of the hepatic artery as a cause of rupture of the liver.

Symptoms and Diagnosis. Teacher and Jack state that in some cases no symptoms referable to the liver occur, but that the aneurysm ruptures before its presence is suspected. In most cases, however, there have been definite symptoms, of which the most common are pain, jaundice and hemorrhage (hematemesis or melena). The striking feature of the hemorrhages is that they

[17] Canadian Med. Jour., July, 1877, vol. vi.
[18] Jour. de Méd. de Bordeaux, 1856, p. 125.
[19] Virchows Arch., Bd. xiv.

recur, frequently with varying intervals between them. It is suggested in explanation that bleeding has occurred into the bile passages and that by rapid filling the bleeding is checked. Severe pain in the right hypochondrium, noted by Rolland just prior to death, is said to have been due to the escape of blood into the substance of liver and the stripping of the capsule of Glisson, rather than to the presence of the aneurysm. In typical cases the pain comes on in paroxysms, and is of great severity resembling that of biliary colic. It is referred to the right hypochondrium and epigastric region. This pain is said to be due to pressure of the sac on branches of the hepatic plexus of nerves. In the case under consideration the pain was sudden in onset and persisted and was probably due to rupture of the intima and consequent tension as sometimes occurs in aortic aneurysm.

Rolland found jaundice in 16 of 40 cases and felt that it was due to pressure on the hepatic ducts or common bile duct. In none of his cases was the incidence of jaundice stated to have any relation to the attacks of pain. Grunert found jaundice in 64 per cent. of his cases and explains its presence as due more to blood in the bile ducts than to pressure of the growing aneurysm, though both are probable factors. Grunert, Hale White[40] and Schupfer report cases in which jaundice appeared about the twentieth day following pneumonia. The last observer believes that the sudden appearance of permanent jaundice is significant.

Fever is another symptom mentioned as present in a few cases, sometimes accompanied by rigor, reaching 104° and tending to coincide with the height of the paroxysm of pain. Digestive disturbances are commonly present.

In a case reported by Friedman paroxysms of pain of a neuralgic type were associated with visible pulsation over the liver, occasionally expansible, and accompanied by a systolic shock felt over the ribs. A throbbing sensation was felt later when the attacks of pain had become more frequent. A diagnosis of aneurysm of the hepatic artery was made and at operation the surgeon reported "dilatation and elongation of the hepatic artery" which Friedman insists must be considered an aneurysm, or at least an incipient one.

Bickhardt mentions a case in which a tumor, the size of a child's fist, was palpable under the xiphoid. The tumor became fluctuant and three days prior to death a systolic bruit was heard. A differential diagnosis of echinococcus cyst, carcinomatous metastasis and perigastric abscess following perforation of a gastric ulcer, was considered; the autopsy affording the correct diagnosis of aneurysm of the hepatic artery with rupture into the duodenum. He mentions two symptom groups: (1) Jaundice, pain and hemorrhage; (2) cramp-like pains with a palpable and eventually pulsating tumor with a systolic bruit.

[40] British Med. Jour., January, 1892, p. 225.

Baruch mentions a case in which he had a patient "suffering from cholemia, and internal hemorrhage, and upon exploratory operation, suspecting common bile duct occlusion by tumor or stone, was surprised to find an aneurysm of the hepatic artery." Habs[21] reports a similar mistaken diagnosis in a patient aged twenty-two years, suffering from chronic icterus.

Baruch states that one will think of aneurysm of the hepatic artery when, in addition to pain and icterus, hemorrhage per orem or anum occurs, but mentions that it may be mistaken for cholelithiasis or duodenal ulcer. "A differential diagnosis is based on (1) young age, (2) male sex, (3) previous infectious disease, especially pneumonia. If the three cardinal symptoms (pain, icterus and hemorrhage) are missing then a differential diagnosis is impossible and the only way to find out would be exploratory incision."

Reichman reports a case associated with pain and hemorrhage, apparent at mouth and anus, but bruit and pulsation were lacking so "no diagnosis was possible."

Treatment. Of 41 cases collected by Baruch only 8 were operated upon and of these but 4 were correctly diagnosed even at operation (Habs, Allesandria,[22] Tuffier and Kehr[23]). In addition Baruch reports a case in which the diagnosis was made by exploratory incision but fearing liver necrosis he did not ligate the artery. The patient died with symptoms of heart failure. Habs took the same view in his case and performed cholecystectomy and tamponade on the sac. Allesandria incised the sac and tried to stop the bleeding by tamponade but the patient died of exhaustion. Kehr ligated the artery and his patient recovered and he therefore concluded that "every case of aneurysm of the hepatic artery should be ligated, because there is a collateral circulation which has formed during the formation of the aneurysm." Tuffier also ligated; his patient died after passing into coma on the third day following operation. No liver necrosis was present. He believes slow obstruction permits sufficient anastomotic circulation and considers ligation of the hepatic artery the operation of choice.

Baruch cannot accept Kehr's conclusions, stating that experimental work on animals has shown that liver necrosis may occur, quoting Naroth as saying that ligation of the hepatic artery must depend upon the site, "the more central the ligation the more the possibility of recovery." Thus he shows in animals that ligation of the common hepatic artery permits a good anastomotic circulation by the right gastric and gastroduodenal arteries. This is nicely born out in the case reported by Merkel—in which an aneurysm of the common hepatic artery occluded by thrombus permitted a sufficient circulation by means of the vessels named.

[21] Deutsch. Ztschr. f. Chir., 1904, lxxxi, 158–178.
[22] Bull. d. l. Acad. med. di Roma, 1906, xxxii, 63–76.
[23] München. med. Wchnschr., 1903, i, 1861–67.

Baruch summarizes by stating that "a sufficient collateral circulation is present when, if the blood supply of the hepatic artery is ligated or compressed temporarily, a puncture of the aneurysmal sac still continues to deliver blood." If the phenomenon is negative he advises (1) the formation of adhesions by scarifying the posterior and lower part of the liver, and (2) compression of the aneurysmal sac.

Zesas[24] in a lengthy discourse on the subject concluded that ligature in any part of the hepatic artery seems the only rational therapy once the diagnosis is made.

Anderson reports a case with operation and recovery in a young man having a previous history of aneurysm of the radial artery. The patient was taken to the hospital in a state of collapse; the abdomen was opened, two quarts of clotted blood removed and a very perceptible oozing noted, welling up in the right lobe of the liver. The hemorrhage was controlled by two mattress sutures and a gauze pack. He states that the hemorrhage undoubtedly occurred from a branch of the hepatic artery. The patient made a very good recovery and with specific treatment gained 30 pounds in four months, only later to develop an aneurysm of the tibial artery and still later gangrene of the toes necessitating amputation.

Summary. 1. Aneurysm of the hepatic artery is a very unusual condition, but 55 cases being recorded in literature.

2. It is of unique origin; infectious diseases playing a larger part in its etiology than syphilis.

3. The main clinical features are pain, jaundice and hemorrhage. Rarely are tumor or bruit present and then only in the terminal stages.

4. Under favorable circumstances the treatment is ligation of the hepatic artery.

PRIMARY SARCOMA OF THE APPENDIX: A CASE OF LYMPHOSARCOMA OF THE APPENDIX WITH ACUTE INTESTINAL OBSTRUCTION IN A YOUNG WOMAN. A REVIEW OF THE LITERATURE.*

By Hyman I. Goldstein, M.D.,

CAMDEN, N. J.

Thiersch, in 1882, reported the first case (none found previously recorded in the medical literature of the world) of malignancy of the appendix. Thiersch's case was an adenocarcinoma at the junction of the appendix and cecum. This case is described in *Berlin*

[24] Fortschr. d. med., Berlin, 1910, xxviii, 1313, 1351–1390.

* Read before the Pathological Society of Philadelphia, June 10, 1920, and the Northern Medical Association of Philadelphia, October 8, 1920.

klinische Wochenschrift, 1882, i, 41. However, primary carcinoma was first recognized and described by Merling in 1838. Many cases of primary carcinoma of the appendix have recently been reported in the literature of the world. There are now on record about 325 cases of primary cancer of the appendix in the entire literature. Primary carcinoma of the appendix is still comparatively rare. Harte in his article states that primary cancer was present in one-third of 1 per cent. of all cases operated on for chronic appendicitis. In 7000 specimens examined up to a few years ago at the Rochester Clinic there was not one case of primary carcinoma of the appendix. Milner believes a condition often recorded as carcinoma is the result of inflammatory proliferation of the adenomatous and endothelial structure of the appendix. Orth and Borst have also pointed out that carcinoma-like formations may follow inflammatory proliferation of such tissues. The majority of cases of primary malignant disease of the vermiform appendix have been recorded since Harte, in 1908, in the *Annals of Surgery*, published a review of all the cases of malignancy to date of writing. He collected, at that time, 120 cases, 114 being carcinomata and 6 sarcomata. Meyer has recently (1915) collected 269 cases of primary carcinoma of the appendix. However, cancer of the vermiform appendix is less frequent than this number indicates, because at the Nicholas Senn Hospital out of 2000 cases one malignant appendix was found, and this was a round-cell sarcoma reported by Michael Wohl, of Omaha, in 1916. Stanley P. Reimann, pathologist of the Lankenau Hospital, Philadelphia, reported 12 new cases of primary carcinoma of the appendix and the 5 previous ones out of a total of 13,151 specimens or about 0.13 per cent. MacCarty and McGrath report 40 cases of carcinoma in 8039. Geist recently reported some rare pathologic conditions of the appendix. Powers in his article mentions the 5 cases Harte described in his paper as sarcomas; Carwardine's (2), a man and a woman; Paterson's (man, thirty-five); Warren's (boy); Guilford's (woman, twenty-seven), and adds his own case (girl, seventeen) and those of T. G. Davis (man fifty-one) and de Jong (adult male). Authentic cases of endothelioma of the appendix have been reported by Glazebrook, Sargent and Sudsuki. Powers reports as questionable the "Sarcomata" of the appendix recorded by Sonnenburg, Murray and Beatson, and concludes by saying (October, 1910) that "Warren's case (in a boy) is practically the only successful case in the series, which, including the case of the writer, numbers 7 instances of primary sarcoma of the appendix."

W. G. Nash reports a giant mucocele of the appendix; M. Cazin, *Des tumeurs endocrines de l'appendice;* carcinoid appendix by Nicolaysen; Bobbio reports a primary carcinoma of the appendix. Crouse in his excellent review of the subject mentions sarcomas of the appendix reported by Sonnenberg, Lamers and Moschowitz and

two myosarcomata by Moschowitz. Boyer reviewed the literature and reported a case of primary carcinoma in 1919.

Cases of primary carcinoma have recently been reported by Darling, Jessup, Macewen, Vance, Tuxen, Braagst, Lahm, Norrlin, Rassieur, Ries, Nigst, Goldstone, Suzuki, Beatson, Mikenda, Bender, Luce, Markoe, Meyer, Ross, Solling, Maresch, Barclay and many others. Rokitansky, Prus, Merling, Mayal, Lichenstein, Leman and others reported cancer of the appendix many years ago.

Primary sarcoma of the vermiform appendix is a great rarity. Up to 1908, Harte, of Philadelphia, was able to find only 6 cases recorded in the entire medical literature of the world, after a very careful search. Garnett Wright, of Manchester, England, in 1911, found 2 other cases, and 1 he recorded, making a total of 9, including Jones's case. In the November, 1910, issue of *Surgery, Gynecology and Obstetrics*, page 466, 11 sarcomas are listed, including 3 doubtful ones.

The first authentic case was reported by Hastings Guilford before the (England) Reading Pathological Society in 1893. This was a case of sarcoma surrounding a concretion in the vermiform appendix. Excision of the cecum was followed by recovery. The patient was a young married woman, aged twenty-seven years. She was always subject to constipation. She was operated upon February 13, 1893. She had three distinct attacks of pain: First in August, 1892, temperature with vomiting and fever (101°). It was thought to be due to uterine cramp. January 30, 1893, she had another attack, with pain around the umbilicus. In this case inflammation existed around the appendix for thirteen years, of a chronic nature.

The first case in America was recorded by J. C. Warren in 1898. Up to Jones's case, 8 cases in all had been reported in the literature, 4 of which were reported in this country.

Jones's case (Seattle, Washington) occurred in a young married woman, aged twenty-six years. She had a mild, recurrent appendicitis, and because of adhesions already existing, extended from the appendix to the walls of the cecum. The patient recovered. Recurrence occurred in Carwardine's case, (1907) here the cecum was also involved. Michael Wohl, of Omaha, reported a case of round-cell sarcoma of the appendix (1916) occurring in a man, aged thirty-five years, a drug clerk. Ten cases, including Jones's, Powers's and Glazebrook's cases were reported up to the time of Wohl's writing, or a total of 11 cases (with Wohl's case) of primary sarcoma of the appendix recorded in the entire medical literature of the world. Wohl, however, did not list White's case (1913); nor those of Davis, de Jong, Smit and Wright—a total of 5. Wohl's case was confirmed by Dr. Frank Hall and M. Petit.

L. Smit reported a case of sarcoma of the appendix in a soldier, aged forty-four years, in the *Medical Review*, Bergen, 1916, xxxiii, p. 377 (Norway). The case of de Jong (1908) occurred in an adult

male. The appendix contained a small fecal concretion in its central portion and at its tip there was a tumor the size of a hazelnut.

Powers's case (Denver) was reported before the Colorado Medical Society at Colorado Springs, October, 1910 (by Dr. Charles A. Powers, of University of Denver). This case occurred in a young female patient (Miss B.), aged seventeen years. She suffered from a fairly typical attack of acute appendicitis five weeks before operation. Lost fifteen pounds in five weeks. She was again seized with a sudden attack of abdominal pain, and vomiting repeatedly. W. B. C., 14,000; operated upon on March 15, 1910. Appendix examined by H. S. Denison, of St. Luke's Hospital, and confirmed by Dr. William Welch, of John Hopkins Hospital, Baltimore. She steadily lost flesh. Systemic injections of Coley's toxins were given for the general sarcomatosis which resulted from the initial growth. Patient died May 23, 1910, ten weeks after operation. T. G. Davis's case occurred (1900) in a man, aged fifty-one years. He had suffered for twelve months. After operation it was found to be a small round-cell sarcoma. In his paper Wohl excludes Glazebrook's case (endothelial sarcoma) because he thinks it probably an inflammatory tumor resulting from proliferation of the endothelial lining of the lymph spaces. Kelly and Hurdon ruled out the case of Guilford and Rolleston, and Jones excluded Bernay's case. However, Wohl includes these last 2 cases in his total of 10 cases of sarcoma of the vermiform appendix found recorded in the entire medical literature of the world. Warren's case occurred in a child, aged six years. Carwardine's first case was a female patient, aged forty-five years, the other occurred in a man, a case of primary lymphosarcoma of the appendix. Bernay's case was twenty-nine years old, a female patient. Paterson's case was a man, thirty-nine years of age, round-celled sarcoma. Glazebrook's case was a colored man, fifty-five years of age. In (George D.) Stewart's case the man was thirty-five years old, had his first attack of appendicitis a year before operation; he had pain over the appendix, a second attack three months before operation and a third attack two months later. On the day of operation he was taken with severe pain and persistent vomiting. W. B. C., 16,000 to 12,200. Operation, February 1, 1908. Harlow Brooks made the examination and the pathologic report of Stewart's case and called it fibrosarcoma (spindle-cell sarcoma).

Nothnagel does not note a single case of primary sarcoma of the appendix. Jones, of Seattle, says: "It is an extremely rare occurrence." In Warren's case the patient was well and free from recurrence four years after operation. This is striking evidence of the apparent slight malignancy (at times) of these growths as compared with those in all other parts of the alimentary canal. Results of operation, both immediate and remote, have been good. Inflammatory changes, either chronic or acute, very frequently

accompany the growth. The fact that primary sarcoma of the appendix may take its origin in an inflammatory process forms a very strong additional argument (Wohl) for the removal of all appendices which show evidences of inflammation. Zaaijer comments upon the preceding existence of chronic appendicitis as an important factor in the etiology of malignancy of the appendix. He also calls attention to the youth of the patients. In the very few cases reported (17) the tumor has been comparatively small and the diagnosis was made only by microscopic examination of the specimen. According to White and Whaland it has been difficult to state whether these tumors have accompanied an inflammatory process or followed it, or whether they have resulted from an entirely independent process (sarcoma) that has later caused inflammatory change. Sarcoma is classed as a connective-tissue tumor, but unlike other connective-tissue tumors the cells do not advance beyond their embryonic state but multiply as such. Wright, in his analysis of the 9 cases recorded at that time, states that in a majority of the cases the growth was a round-cell sarcoma, 4 classified as round-cell sarcoma and 2 as lymphosarcoma. He suggests that it is possible that all were really examples of lymphosarcoma; 1 was called an endothelial sarcoma and 2 were classified as fibrosarcoma or spindle-cell sarcoma, but in both these latter cases inflammatory changes were present and the diagnosis seems to be doubtful. Wright's case occurred in a boy, aged seventeen years (January, 1909), recovered, and in good health two and a half years after operation. Wohl states prognosis in sarcoma of the appendix is less favorable than in cancer, while in the latter metastasis and recurrence is the exception, in sarcoma only 3 cases have remained free from recurrence, 4 cases have developed recurrence followed by death and 1 case died six hours after operation. He concludes sarcoma of the appendix, especially the round-cell type, is highly malignant; and that it is a rare condition—only 10 cases recorded in the entire medical literature of the world.

In 840 appendices examined at the Episcopal Hospital, Philadelphia, from January, 1918, until the time of writing the 1913 reports, one case of sarcoma of the appendix had presented itself. White's case occurred in a young woman, E. F., aged twenty-five years. Her chief complaint was abdominal pain and vomiting. Operation, September 18, 1909, by Dr. Harry C. Deaver. According to White and Whaland's analysis (1913) the type of cell found in the reported cases varied, viz.; small round cell, 8; spindle cell, 3; lymphosarcoma, 1; fibrosarcoma, 1; small round cell (White's case), 1.

Hugh Crouse, of El Paso, Texas, reviewed to 1910 the literature on "Tumors and Retention Cysts of the Appendix," and mentions and lists all the cases of carcinoma, sarcoma, myxoma, fibromyoma, cysts and myosarcomata of the appendix that he found in the

literature up to 1910, since the first malignant appendix was recognized and described by Merling in 1838.

Clarence Webster, H. A. Kelly, Moschowitz, Goffe, Isaac, Coons, Wahlgren, Letulle, A. O. J. Kelly, E. H. White, McWilliams, Zaaijer, Wolskler, Burnam and Le Conte reported cases of primary cancer of the appendix. Fischer, Reel, Parker, Chevier, Moore and Palieri reported cystic tumors of the appendix; Ogilvie, a pseudomyxomatous cyst; Phemister, a pseudomucinous cyst; Stickney, a myoma; Tyler, a colloid cyst; Beatson, carcinoma in a girl, aged twenty years; J. Halban, carcinoid growths; Ombredanne, aged eight, a myxoma; L. D. Redway, a leiomyoma; Tagliavacche, fibromyoma and actinomyces; Moore, cysts; Bailey, pseudomyxoma; Battle, sarcoma of ileum in a girl aged eight years. Carwardine treated his patients in 1905. Shattock, who examined the specimen, called it lymphosarcoma, having its primary origin in the submucous tissue and tending to infiltrate the neighboring coats, as is common with lymphosarcoma of the alimentary tract. He mentions Paterson's and Warren's cases as the only 2 found recorded in the literature to 1907, and quotes H. D. Rolleston and Lawrence Jones to that effect. Crouse lists the following cases and articles on the subject of sarcoma of the appendix, including some that have not been accepted, being considered as questionable by various writers: Sarcoma, H. A. Kelly, 5 cases (mentioned in his Book, 1905); Lamers, 1 case; A. C. Bernays, 1 case; Sonnenberg, 1 case; Moschowitz, 2 cases; Guilford, 1 case; Rolleston and Jones, 2 cases; Warren, 1 case; Carwardine, 1; Paterson, 1 case; Moschowitz (myosarcoma) 2 cases.

At the Mt. Sinai Hospital, New York City, up to June, 1908, there were examined 2700 specimens, and among these were 8 cases of primary carcinoma of the appendix. He (Moschowitz) mentions as "peculiar" about carcinoma of the appendix that they occur in the very young, and he mentioned before the New York Obstetrical Society at the time of this discussion a case in a young girl, aged ten years.

The diagnosis of sarcoma of the appendix cannot be made in the early stages from the symptoms. All the cases resembled attacks of appendicitis. The prognosis is good if the tumor is small and situated some distance from the proximal end of the organ, and when adhesions and involved glands are not present. Sarcoma of the appendix is usually of the small round-cell type, which is generally of rapid growth, infiltrating and tending to rapid metastasis. The adjoining head of the cecum and the draining lymphatic glands should always be very carefully examined and their condition determined. In about one-half of the malignant appendices (carcinomata and sarcomata) the growth is found at the distal end of the appendix. Most of the patients are young, the greater number occurring in the female.

Treatment consisted of simple appendectomy and resection of enlarged glands of the mesoappendix when malignancy of the cecum and appendix was suspected by the surgeon. Le Conte mentions the fact that simple removal of the appendix (cancer) is sufficient to bring about a cure. The good results are explained by Crouse as probably being due to the early symptoms and early operation in primary malignancy of the appendix vermiformis. Wells comments on the youth of the patients and states that he was able (1908) to find only one case which had died of carcinoma existing only at the appendix.

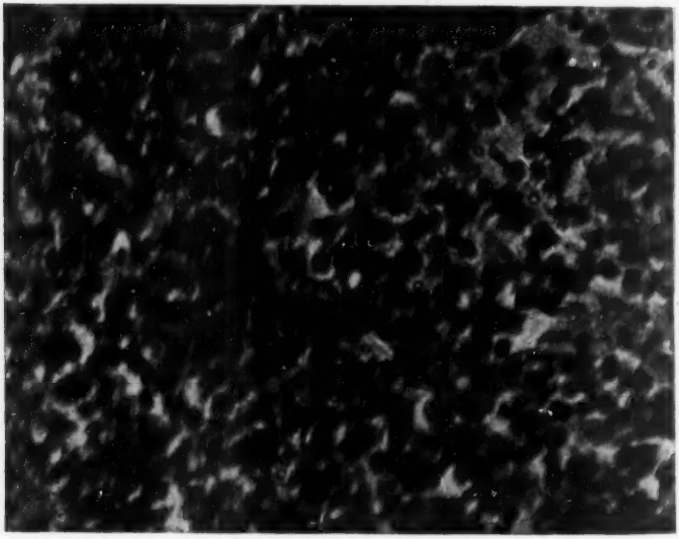

FIG. 1

Case Report. Miss Lena G., aged twenty-five years; white girl. Resides in Camden, New Jersey.

Family History—Negative. Worked in pen factory for a number of years. I was called in to see her for the first time on September 29, 1919, at 10 P.M. She said she was an inspectress of pens and was piercing the slits and cuts in pens for eight years. She was always very constipated and had "stomach and bowel" complaints for several years. She had swollen feet and legs several years ago; had measles and "rheumatism." Lost 23 pounds in the past two years, most of it during the past few months. Her best weight was 123 pounds; now weighs only 100 pounds. She has had several similar attacks of "appendicitis," with severe pains, abdominal cramps and vomiting during the past four or five years. Present

attack of "pain in the stomach" and vomiting began two days ago, and a physician who was first called in diagnosed the case as acute appendicits. The vomiting was persistent and severe and the pain became worse. Abdomen was distended and rigid; pulse rapid; temperature, 100.5°; patient looked "very sick." There was a peculiar fulness and distention in the upper abdomen, and marked pain and tenderness and rigidity very low down in the right iliac fossa. While the case gave all the appearances of a severe acute appendicitis, with probable abscess formation and adhesions due to previous attacks of inflammation in this region, yet it also looked

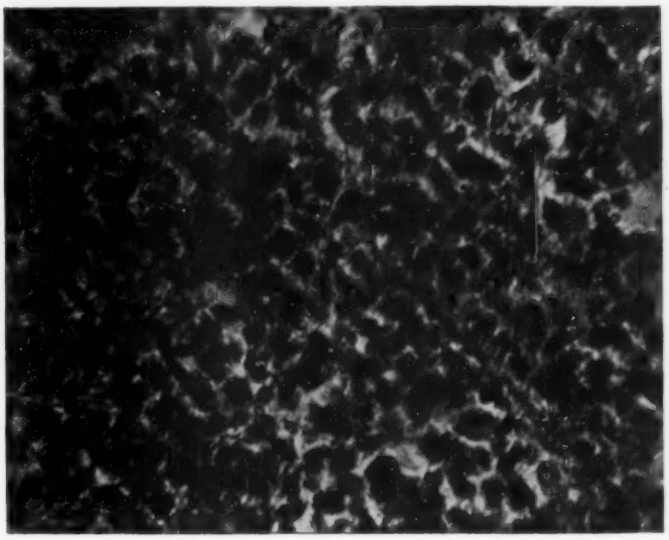

FIG. 2

like a typical case of acute intestinal obstruction, with or without some acute inflammation, and involvement of the right tube and ovary. I advised immediate removal to the hospital for operation. The patient and her family wanted to talk it over, during the night, so I left the house. Early the next morning, September 30, 1919, I was urgently called on the telephone, to come to the house at once, as the patient was much worse, the pain more severe, and the vomiting constant. I found the patient in bad shape, with markedly distended and painful abdomen. I immediately arranged with Dr. Alfred C. Wood, of the University of Pennsylvania and Howard Hospitals, Philadelphia, for prompt operation. Dr. Wood saw her, within two hours after I left the patient's house, at the Howard Hospital. He also thought there may be intestinal obstruction

with the diseased appendix. Under ether anesthesia Dr. Wood opened the abdomen and found the appendix diseased, with a mass involving the appendix and the head of the cecum; the mass in the cecum could be distinctly felt, but was thought and hoped to be inflammatory in nature. Appendectomy was quickly done, as the patient was very weak, and the cecum left untouched for the present. The gut was markedly congested and distended with gas and forced outside of the incision. On searching for a possible obstruction a thick band was found tightly constricting the gut low down in the right iliac fossa, and a foot of bowel was dark and quite

FIG. 3

discolored; the strip where the band was holding was nearly black and gangrenous; however, upon release of the band and the application of hot wet compresses, the color improved, and as the patient was very weak, Dr. Wood and I felt enough had been done; the distended gut was therefore, with some difficulty, replaced into the abdominal cavity and the wound sewed up, and the patient was returned to her private room. The appendix was sent by Dr. Wood to Professor Allen J. Smith, pathologist of the medical department of the University of Pennsylvania, and he made a very careful examination of the tumor and the report of lymphosarcoma of the appendix was received from him (October 21, 1919, Block, No. 6239), and is here appended. The "mass" in the cecum cannot be felt at present (May 26, 1920); this was probably inflamma-

tory in nature, and probably not the same as the real tumor in the appendix. The patient is well and able to do her work, eight months after the operation. She has not regained her best weight and is still very costive. She has no pains and feels "no mass." Has no cough nor chest symptoms, no palpably enlarged lymph nodes. She says she weighs about 100 pounds and has some abdominal distention when "her bowels do not move for a day or two." Her mother recently had an attack of biliary colic; she is fifty-three years of age and has had "gall-stone trouble" for twenty years. I saw the patient and her mother May 26 and June 1, 1920.

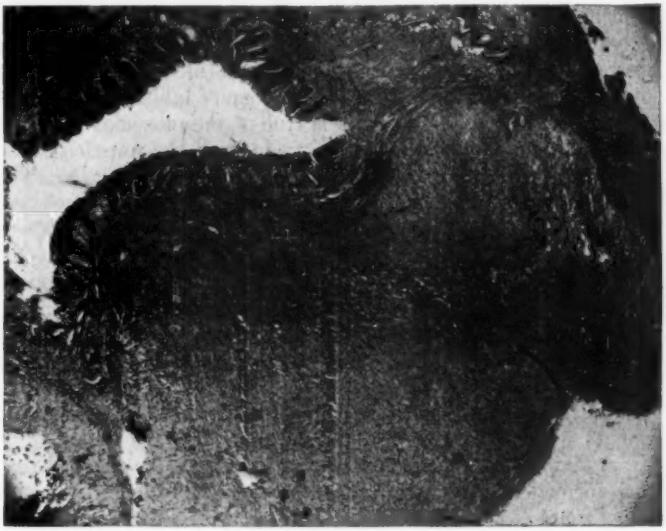

FIG. 4

Report of Specimen Examination. Name and address of the patient: Lena G., Camden, N. J.

Diagnosis: Lymphadenoid sarcoma of the appendix.

Section of appendix in proximal, thickened, portion above the tube here of approximately 1 cm. in diameter, the thickening involving to some extent all of the circumference of the wall, but particularly that half next the mesoappendix, which is over 5 mm. in thickness (that of the opposite side being about 1.5 to 2 mm. thick). The lumen in the section is open but compressed by the swollen side of the wall to a crescentic outline. Under low magnification (under a hand lens) the thickening referred to seems due to a fairly defined mass under the broken mucosa, apparently involving both submucous and muscular coats and extending into a thickened meso-

appendix. With higher magnification this mass is found fairly sharply defined but not encapsulated, and to be composed of small round cells of lymphocytic type, not arranged with any special architecture, infiltrating the deeper tissues, but apparently partly limited to the overlying mucosa. At its borders the cells infiltrate the adjacent tissue of the submucosa and deeper coats; and in its extension through the wall it infiltrates the muscular coat irregularly.

The mucosa is relatively normal, broken at one or two points by artefact and not ulcerated; its glands of about normal size and showing a slight excess of goblet cells. Its follicles are large, solidly lymphocytic; and at its base throughout the circumference there is a continuous excess of lymphoid cells, suggestively extending from the lymphocytic mass above referred to. In the half of the wall not occupied by the nodule the submucosa is thickened, fibrous but loose, with the node showing a narrow zone of infiltration on each border into the coat. The same is true of the muscular coat and of the fibroserous tunic, but in the node itself the muscle can be traced, its fasciculi separated well by the lymphoid cells. The fibroserous coat is dense and slightly thickened at places, elsewhere thick and loose as from edema, and throughout contains a scattered excess of lymphocytes.

There is a second section of a loose fibromuscular tissue (smooth muscle) which is believed to have been part of the mesoappendix, which does not show the structure of intestinal (colon or appendix) wall. In this as well the lymphocytic formation is massively infiltrated in part of the tissue, the rest of the tissue showing a loose, rich infiltration by the same type of cells and small foci of the same elements.

In studying this lymphocytic formation it is to be recalled that it has formed in one or more nodules, not encapsulated but with narrow zones of infiltration at the borders, with scattered excess of the same type of cells through practically all of the sections; that it does not present the architecture of a normal or of an inflamed lymph node, being without follicles and sinuses; that the cells are contained in a delicate lymphadenoid reticulum. The cells are almost all of the ordinary appearance of small lymphocytes, but scattered among them are larger lymphoid examples, and that at places there is the appearance of elongation of these cells into spindle form and small fibroblasts as if some degree of organization were proceeding at such sites. There are too at places eosinophiles to be seen. The small mass is fairly vascular, the vessels of capillary type.

From the above data the writer is satisfied that there is a chronic inflammatory involvement in the changes of the appendix, but believes that the nodular thickening on one side of the appendicular wall is not of inflammatory origin, not to be a lymph node occurring aberrantly in this situation, but by exclusion has come to the view that it is a true tumor, a lymphadenoid sarcoma.

Conclusions. 1. While carcinomata of the appendix have been more frequently reported during the past fifteen years, they are still comparatively rare.

2. Sarcoma (primary) of the appendix of any type is a very great rarity.

3. That the following are the only authentic and accepted cases of primary sarcoma of the appendix found recorded in the entire medical literature of the world: Those of Guilford, Warren, Patterson, T. Carwardine (2 cases), de Jong, T. G. Davis, Powers, Rohdenburg, Wohl, Smit, White, Stewart, Jones, Bernays, Wright and the author's case—a total of 17 cases, if we accept all these cases, and exclude Glazebrook's case, of sarcoma of the appendix in the entire literature of the world.

4. All the cases showed symptoms resembling attacks of acute or recurrent appendicitis. It is impossible to make a correct diagnosis before operation.

5. All appendices removed at operation and at autopsy should be carefully examined; there may be more malignant appendices found which at present escape, because of failure to examine them carefully in the laboratory.

I wish to express my thanks to Prof. Allen J. Smith,* for the preparation and the careful examination of the slides and for making the three illustrations (photomicrographs) and the complete report; and to Dr. A. C. Wood, for the prompt operation, and for sending the specimen to the medical laboratories of the University of Pennsylvania for study immediately after the operation.

Addendum: Primary Sarcoma of the Appendix. Rohdenburg of the Lenox Hill Hospital, New York City, has reported a case of primary lymphosarcoma of the appendix occuring in a child, aged four years. In his report before the New York Pathological Society he stated that after a thorough search of the literature he found his to be the "first case of a lymphosarcoma of the appendix." Ten months after the operation the patient is still alive and apparently healthy. No other evident tumor process was found in the abdomen at the time of the operation. Microscopic examination showed a typical lymphosarcoma involving all the coats of the appendix extending into the mesoappendix and infiltrating the cecum. The growth showed the usual signs of an acute suppurative infiltration.

Brinkmann, on November 16, 1920, before the St. Agnes Hospital Clinical Society, Philadelphia, reported a case of primary sarcoma of the small intestine. While the appendix was not found to be seriously involved, the actual mass consisting of a hard, flat growth was found about three inches from the ileocecal valve, which produced (partial) obstructed interference to the passage of the bowel contents.

* Prof. Joseph McFarland, Prof. Milton B. Hartzell and Dr. Frank B. Lynch, of the University of Pennsylvania, also examined the slides and confirmed the diagnosis.

The patient was a child, aged eight years, who had three attacks of what appeared to be acute appendicitis, with recurring attacks at intervals of two weeks. Dr. Brinkmann saw the patient with Dr. Blumberg in the third attack. Diagnosis was made of acute appendicitis, probably gangrenous, the appendix enveloped with omentum. At operation the appendix was found not to be seriously involved. The mass, situated three inches from the ileocecal valve, was resected. No other demonstrable lesions were found in the abdominal cavity. The operation was performed on February 22, 1920. The patient made an uneventful recovery. Her general appearance indicated health. She was of normal stature for her age and of normal weight. At present, nine months after the operation, abdominal examination is negative. Roentgen-ray examination made at the St. Agnes Hospital is also negative. The passage of an opaque meal was uninterrupted.

Brinkmann states that while it is true the time is too short to predict a complete recovery without recurrence, he feels from the pathologic examination that her chances are bright. The section as shown under the microscopic examination, demonstrates invasion of the mucus and submucus coats only, the peritoneal coat being normal at the periphery of the resected portion of the gut.

NOTE.—Dr. Brill, of the Mount Sinai Hospital, New York City, some time ago, at a meeting in Albany, reported a case of sarcoma of the duodenum which disappeared spontaneously. Dr. Stengel, of the University of Pennsylvania Hospital, Philadelphia, told me of an interesting case he had in a woman, aged thirty-five years, in whom at operation a large sarcoma of the stomach was found, the stomach wall being over three inches thick. In both cases they were thought to be *primary sarcoma* of the gastro-intestinal tract.

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INFLUENZA AND EPILEPSY: FURTHER STUDIES UPON THE RELATIONS OF MENTAL DISEASE AND INFLUENZA.

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What effect has influenza upon idiopathic epilepsy?

Hippocrates is cited as saying that "acute fevers can influence epilepsy both favorably and unfavorably."[3] Of course, Hippocrates did not know of influenza, or at least not by its present name or reputation. When one recalls that acute infections have sometimes seemed to improve or even cure epilepsy, as well as some psychoses[23] and even hypophrenia,[35] it is the more pertinent to inquire if, after all, the influenza epidemic may have accomplished at least this morsel of good or if, on the other hand, it was as we supposed, "An ill wind that blows . . . etc."

Yet, strangely enough, the matter has never aroused much interest. Literature on the topic is remarkably scant. There were a few scattered communications on the general subject of epilepsy associated with the influenza epidemic of thirty years ago, and to date one[10] discussion of the subject in relation to the 1918 epidemic and one case report; the interim is barren.

Study of the question is facilitated by the large amount of material afforded by the epidemics of influenza of 1918 and 1920. Intramural ravages of the epidemic were experienced in most of the institutions for the care of epileptics in this country. Questionnaires addressed by the writer to the superintendents of these institutions were very courteously treated and the responses were gratifying. However, the severe crippling of the medical staffs as well as of the employee force as a result of war, influenza and price inflation made impossible the detailed notes and observations which would have been desirable. Pertinent data and cases from these replies are cited. In addition to these data I have certain cases for report taken from our Boston series[2] (the Psychopathic Hospital), from which we have presented previous studies of the relations of influenza and mental disease. I have emphasized[35] that it is not because influenza is so important *per se* that its relations to mental pathology have been thus the object of our persistent analysis, but because influenza furnishes us with a ubiquitous and tangible somatic factor.

The exact status of the somatopsychoses is perhaps as tenuous as that of any of the major groups of mental disease, and it behooves us to regard, with an extraordinary interest, any data available to further our knowledge concerning the interrelations of mind and body; or, better, of brain pathology and body pathology. What little has been achieved in this direction in the past has been done

by similar studies of typhoid fever, malaria, etc., diseases which could never compare in ubiquity with influenza, and which, thanks to the efforts of preventive medicine, are so rapidly decreasing as to be no longer sources of psychiatric study.*

Delasiauve[4] as early as 1854 considered the subject of epilepsy and acute infections. He discusses the influence of various infections, *omitting influenza*, and decides for a specific effect for some (*e. g.*, erysipelas, he thought, improved epilepsy, whereas typhoid augmented the manifestations). He cites many writers and many cases of his own, and concludes in general, on this point, that "all severe and acute illnesses suspend or weaken epileptic fits and chronic ailments diminish them." Veysset[5] undertook a detailed historic review and cites 6 cases, but nowhere refers even indirectly to influenza. Seglas[6] wrote at length concerning the influence of almost every sort of thing upon epilepsy—measles, scarlatina, fractures, erysipelas, malaria, etc.—but he nowhere makes mention of influenza. Certain of his conclusions are worth quoting here, however, even with this pertinent omission: "Intercurrent maladies have in the majority of cases a favorable influence upon the course of epilepsy. . . . This influence may not be manifested during the course of the intercurrent disease. . . . The acute diseases with febrile reactions bring about the most perceptible modifications."

Perhaps the most spectacular account of the effect of febrile affections upon epilepsy is that of Turnowsky,[7] of Marosvasarhely, who cites 3 cases of established epilepsy in which seizures were never again seen (six to fourteen years' observation) after attacks of pneumonia (two) and scarlatina (one). He is enthusiastic enough about these observations to suggest the possible therapeutic advantage in epilepsy of exposure to scarlatina or pneumonic infection.†

Upon recourse to the text-books one is again disappointed. Oppenheim[8] remarks that "acute febrile diseases often serve to inhibit the convulsions (of epilepsy), and recovery may even in a few cases be due to this cause." But his only mention of influenza in this regard is to cite (upon another page, 1215) an instance of reprecipitation of attacks, to be referred to later. Most of the writers are content to make some such ambiguous statement as

* Recently Paulian[25] has made a detailed study of typhus fever; Skoog[27] recently reported briefly on measles. There has been rather more tendency of late toward psychiatric analyses of the endocrinopathies such as Raeder's[28] recent report on the endocrinopathic aspects of feeblemindedness. All of these efforts are valuable because they give us additional data in the consideration of the broader question of somatopsychoses as a group.

† Whatever opinion one may form of this proposal, Turnowsky's suggestion of the possible application of the analogy of the phenomena of reinforcement and interference of the waves of light and of sound to the intercurrence of pathological entities is worthy of attention. The great principle of analogy is rather likely to be applied, we think, too closely within the separate (?) spheres of scientific study, and this wide flight of Turnoswky's, for all its novelty, certainly has merits of originality and perhaps of faithfulness.

this, from Paton:[9] "The relation of the acute infectious diseases to this psychosis (epilepsy) has been repeatedly emphasized by clinicians—measles, diphtheria, typhoid, as well as whooping-cough, scarlet fever and malaria."

I. Evidence That Influenza May Improve Epilepsy.

That there is often observed a cessation of attacks during the height of the acute illness has been commented upon by various writers, some of whom have been quoted. Maillard and Brune,[10] in addition to pointing out the increased susceptibility of epileptics to influenza, put emphasis upon the "almost complete suppression of attacks during the period of acute (influenzal) illness" in all their cases. They found that the average total number of attacks was lowered from 105 daily prior to the epidemic to 14 attacks daily during the febrile period. "The curve of attacks in the course of the influenzal infection is absolutely characteristic in all of our observations, an arrest of the epileptic by the influenzal process."

Similar observations were made in this country. Dr. H. B. Carriel, managing officer of the Dixon (Illinois) State Hospital, replied to the question of the effect of influenza upon the epileptics in his institution as follows:

"It was not found that the disease had any permanent effect upon the epileptics. It was noticed, however, that of those suffering from influenza almost none had seizures (of epilepsy) during the attack (of influenza). This was especially true during the time that their temperatures were abnormally high or subnormal."

This fact is also pointed out in a letter from Dr. David Fairchild Weeks, superintendent of "The Village for Epileptics," at Skillman, New Jersey. "During the time the patients had a rise in temperature they did not have convulsions."

The following case is one studied at the neurological clinic of the Boston Dispensary (then in charge of Dr. Abraham Myerson), where the writer was an assistant visiting neurologist. The case is reprinted in abstract from a previous communication dealing with mental diseases associated with influenza.[11]

Case 1.—*Family History.* A white school boy, aged fourteen years, had a father who was subject to outbursts of temper, and a mother who was subject to chronic headaches. One sister is living and well.

Past History. Unimportant.

Epileptic History. In August, 1916, he had a sudden epileptiform seizure, quite typical in form. They recurred frequently thereafter, averaging one a month.

Present Illness. In September he contracted severe influenza. During his illness he had three, possibly four, more seizures. The

last was on October 21, while he was still bedridden. Thereafter he was seen in the nerve clinic frequently and had no more seizures. (Seen January 14). A physical examination was entirely negative and a Wassermann test on the blood serum was negative.

INSTITUTIONAL DATA. Dr. William T. Shanahan, of the Craig Colony for Epileptics, at Sonyea, New York, in a most comprehensive summary, writes:

"Six patients (one male, five females) had *fewer* seizures *during* the period of influenza and a period of *three weeks before* and *three weeks after* the attack than their usual wont. (This is contrasted with twenty-five patients who had more.)

"Seven patients (all females) had *fewer* attacks per month for the *next nine months after* the influenza than for the preceding months (contrasted with sixteen patients who had more attacks.)"

Dr. Shanahan kindly furnishes the following representative abstracts, as illustrative:

CASE 2.—Agnes S., aged seventeen years, an epileptic for eight years. Monthly average seizures for nine months before influenza, sixteen. During October and November, when she had a moderately severe influenza, ninety-three seizures. Monthly average during nine months following this period, eight.

CASE 3.—J. S., female, aged ten years, epileptic since seven months of age. Monthly average for nine months before influenza, ten seizures. During October and November, when influenza occurred, twelve seizures. Two of these occurred while in bed with influenza. Monthly average of seizures for nine months following influenza, five.

CASE 4.—W. S., female, aged twenty-eight years. Epileptic for twenty-four years. Monthly average for nine months before influenza, six seizures. During October and November, eight seizures, three occurring while ill with influenza. Monthly average for nine months following influenza, four seizures.

For the following 2 cases I am indebted to Dr. O. S. Hubbard, superintendent of the Kansas State Hospital for Epileptics at Parsons, Kansas:

CASE 5.—"Miss H., an epileptic imbecile, has been in the hospital fifteen years. She comes from a defective family. Her seizures usually occur in series at long intervals. She is of the noisy talkative kind, who irritate those about them by persistent conversation. She was extremely sick with influenza, and while she had no distinct pneumonia, had respiratory difficulty. For a number of days her fever remained about 105°, and that gradually subsided. While her fever was high she was much more quiet and talked in a rather

intelligent manner—in fact, seemed another personality, almost normal. With the improvement in her health her mind returned to its former standard and she is in every way much as she was before being sick."

CASE 6.—"Mr. W. had been a patient of the institution for a number of years. For a considerable period he was on parole, and under excessive sedation in the form of patent medicine he became much reduced in health. He contracted influenza which was complicated by pneumonia, from which he made a good recovery. He improved markedly both physically and mentally. One forenoon he had five grand mal seizures in quick succession and following them developed edema of the lungs, from which he died that evening."

II. EVIDENCE THAT INFLUENZA MAY AGGRAVATE EPILEPSY.

Aggravation of epilepsy may be conceived of as taking any of four forms:

1. Simple increase in severity and frequency of attacks.
2. Reprecipitation of long latent epileptic attacks.
3. Alteration in the form of the attacks.
4. Production of a complicating psychosis.

Illustrations of each of these are at hand.

1. INCREASED FREQUENCY AND SEVERITY OF ATTACKS AFTER INFLUENZA. The suppression of attacks of epilepsy during the acute period of illness (influenza) as discussed above is not stated by any of the writers or any of my communicants to have been permanent. So much for negative testimony. On the other hand, Dr. Shanahan writes:

"One patient had status epilepticus during the height of the influenza.

"Twenty-five patients (5 males, 20 females) had more seizures *during the period of the influenza* and a period of three weeks before and three weeks after the disease" (than their average wont). (This is contrasted with 6 patients who had fewer seizures at Sonyea.)

During the *nine months* which have passed since the epidemic 11 males and 5 females who had the disease have shown an increase in the frequency of seizures. (These 16 patients contrast with only 7 who showed a decrease in frequency of attacks.)

Dr. Shanahan also furnishes the following abstracts of cases illustrating the above stated increase in frequency:

CASE 7.—E. Z., female, aged twenty years, an epileptic for ten years. Monthly average for nine months before influenza, twelve seizures. During October and November, eleven seizures. No

seizures while in bed with influenza. Monthly average for nine months following influenza, sixteen seizures.

CASE 8.—E. V., female, aged twenty-two years, epileptic since early infancy. Monthly average for nine months before influenza, twenty-six seizures. During October and November, fifty-two seizures, nine of which occurred while ill with influenza. Monthly average for nine months following influenza, thirty seizures.

CASE 9.—Jacob F., aged twenty-two years, epileptic eighteen years. Average from four to ten seizures monthly for nine months preceding influenza. During influenza period seizures continued with same frequency. During nine months following influenza, seizures were more frequent, averaging thirteen to sixteen per month.

CASE 10.—Albert P., aged fifty-five years, epileptic for forty-two years. For nine months preceding influenza had but four seizures. During influenza period had eleven seizures. During nine months subsequent to influenza averaged two or three seizures each month.

CASE 11.—John R., aged thirty-four years, age of onset unknown. Patient at the colony for twenty years. For nine months preceding influenza, period averaged five to six seizures monthly. During influenza period had fifteen seizures. During nine months following influenza period has had from seven to ten seizures on average per month.

CASE 12.—Charles G., aged thirty-six years, epileptic twenty-one years. For nine months preceding influenza period had average of one seizure per month. During influenza period had twenty-one seizures. Since influenza period had averaged from six to eight seizures per month.

CASE 13.—Fred P., aged thirty-eight years, epileptic since ten years. For nine months preceding influenza averaged ten per month. During influenza period had fifty seizures. During nine months following influenza period has had an average of thirteen seizures per month.

2. REPRECIPITATION OF LONG LATENT EPILEPTIC SEIZURES. Another phenomenon of aggravation is the precipitation of a recurrence of attacks in a patient previously frankly epileptic but in whom supposed recovery or long remission had occurred. This is not infrequently casually referred to in the literature, but I do not know that it is anywhere critically discussed. Oppenheim[8] cites the case of "G, a neuropsychopath," who had suffered from "conditions of anxiety and imperative ideas." "Three times during his

life he had an attack of an epileptic character, once in his seventeenth year after great exertion, one in his twenty-third year after sleepless nights *and one at the age of thirty years after influenza.* In this last attack he was carried home in a state of absolute unconsciousness."

An excellent illustration of this phenomenon is reported by Dr. William T. Shanahan in the communication above mentioned Dr. Shanahan writes:

CASE 14.—"Althea D., aged twenty-three years, who developed epilepsy in infancy and had fairly frequent seizures for some time. She was admitted to the Craig Colony, July 30, 1908, and discharged January 5, 1909, as improved; readmitted December 21, 1911, and discharged January 8, 1915, as recovered, having had no seizures in over two years. In a communication had on July 22, 1919, from this former patient, she stated that subsequent to her discharge from the Colony she had no seizures until after a severe influenzal infection in November, 1918. Since this time she has had frequent attacks, as many as twenty in forty-eight hours in one instance."

Another very similar case of the reprecipitation of epilepsy by influenza occurred in our Boston series and will be presented here. These cases represent latent processes stimulated to renewed activity by the influenza neurotoxins.

CASE 15.—M. W., female, aged thirty-six years, Red Cross canteen worker.

Family History. Negative, except that she was three-eighths Hawaiian, and that a sister had epileptic seizures throughout her life and died at thirty-two after seven weeks of convulsions.

Past History. The patient was an intelligent and cultured woman whose past history was (aside from her epilepsy) simply that of an active and able school teacher. She had held some responsible pedagogic positions, and had travelled extensively.

Medically there was no point of particular interest aside from the present illness and the past epileptic attacks. Her habits were above reproach. Relatives and family physician were interviewed and a long history secured.

Epileptic History. Her first seizure was at the age of sixteen, *following a severe attack of measles.* Nothing further is remembered of this by any informant or the patient. The second attack was twelve years after the first, at the age of twenty-eight, the third two years later and the following year, at the age of thirty-one, she had a fourth attack. The present illness ushered in the next attacks, five years after the one just mentioned.

Present Illness. The patient had not been overwell for some months, partly owing, it was thought, to her supreme overexertion in the cause of the canteen work. One doctor said that she had "subacute appendicitis."

For about a week before admission she was definitely ill. She had had a fever of at least 102° at one time, three or four days prior to her admission, but in spite of feeling wretched and deserving to be in bed, she struggled on with her canteen work. There seems to have been little doubt but that she had influenza.

January 7, at 8.30 A.M., she suddenly had a severe convulsion, repeated at 2 P.M. and 4 P.M., and possibly one other time. She was unconscious after the first seizure: "Knew nobody and could not be taken care of."

Hospital Admission. The patient lay in bed when first seen and to all interrogations responded only with a hoarse groan, often reiterated. She suddenly jumped out of bed, uttering groan after groan, and danced about the room. The nurse led her to the toilet, but she ignored it. She continued her jumping and groaning. She could scarcely be held in bed, and when the nurse left her she crawled on top of the bed, removed her night-gown and squatted nude on her hands and knees, where she remained. Soon after this episode the patient began to clear up and within a few days seemed quite normal, although she was not wholly so for nearly a week.

Mental examination, aside from the points noted, physical examination, neurologic examination and laboratory findings were all negative.

Diagnosis: Series epilepticus, precipitated by influenza.

3. ALTERATION IN THE FORM OF THE ATTACKS. The only case illustrative of this phenomenon is one previously cited in a more general article referred to above and reprinted in abstract here. Noteworthy is the unusual change from the typical convulsive seizures to the somnambulistic or twilight state episodes as well as the increase in frequency of attacks. These cases illustrating the phenomenon of altering type of epileptiform manifestations are infrequent in the literature. I cite (free translations) two cases of Van Deventer's.[16]

A twenty-three-year-old male who, from the earliest youth until three years previously, had suffered from attacks of confusion (Verworrenheit) in which he undressed himself, ran hither and thither, as if seeking something, was brought to the hospital after an epileptic attack in the street, associated with influenza and urticaria. The day before he had felt ill, and as we learned later had had one attack which he himself did not remember. A week later he felt completely well.

A male patient of thirty-six, with slight facial asymmetry, who suffered occasionally from vertigo-epileptica and for the past twelve weeks also from headache, had, one morning before going to work, a severe epileptic attack. He regained consciousness first six hours later and seemed to be suffering with influenza associated with tic douloureux. He knew absolutely nothing of having had an attack, or that he had just come out of one. On the following day he was all right.

My own case now follows.

CASE 16.—Male, aged twenty-two years, single, discharged sailor, born in U. S. A.

Family History. Negative except that one paternal uncle is said to have had epilepsy.

Past History. Normal childhood. He left the high school and joined the U. S. Navy.

Medical History. Unimportant.

Epileptic History. Began at the age of twelve. Thereafter they occurred about every two months until about a few years prior to admission. The attacks entailed the characteristic tonic convulsions, frothing, biting the tongue, etc., but were not extremely severe, and as they were preceded by a somewhat prolonged aura he had never injured himself severely. They were always followed by a period of headache and malaise, with total amnesia for the events of the seizure. For a year or so prior to his enlistment in the navy they had been decreasing in frequency, under the treatment of Dr. Waterman, of Boston.

Present Illness. September 30 he contracted influenza and was in the hospital until November 1. He had pneumonia and was not expected to live. He was delirious during his acute illness and did not remember his father's visits. He had no epileptic attacks during the month (sic).

During November and December he had three attacks. These were of the nature of somnambulism, however, instead of the convulsive type as previously. He was noticed by his employer one day to be mismanaging his duties clumsily and when addressed did not reply, so was taken home where he subsequently recovered without memory for the event. Again, he suddenly left work, taking with him a friend's letter, to which he was in no way entitled, and was observed to stagger as if drunk. The third attack was the event leading to his coming to this hospital. He last recalls being at his work as usual; the police found him wandering the streets in an adjacent suburb of Boston, and, failing in satisfactory replies, he was brought by them here. "In the admission office he has to be prodded with questions frequently in order that any answers may be elicited, and to keep him awake. He said he could not tell where he had been living in Boston the past three years. Later replies that he was a radio student at Harvard."

He was taken to the ward, fell immediately asleep and when seen the following morning was quite clear, but could give no account of the interval between leaving work the day before and awaking in this hospital.

Mental examination, physical examination, and laboratory findings entirely negative. Psychometric test gave rating of 17 plus.

Diagnosis: Epilepsy; twilight state.

4. Production of a Complicating Psychosis. The phenomenon of epileptic psychosis is only one of the recesses of that great mystery epilepsy. Analogous to the psychoses associated with hypophrenia, the psychoses associated with epilepsy are all too little understood. In both hypophrenia[35] and epilepsy, influenza evokes psychoses. In the following instances in every case the epilepsy was of long standing, yet all the stress and strain, haps and mishaps of life had not served to induce a psychotic episode. It surely bespeaks again for influenza the unenviable quality of a most potent neurotoxin.

Dr. O. S. Hubbard, superintendent of the Kansas State Hospital for Epileptics, kindly furnished the following case abstract:

Case 17.—Mr. J., a clergyman, aged forty-four years, graduate of Boston University, had no family taint, but was a nervous individual. When four years of age received a head injury, and now has a small depression of the right motor area. About eight years ago, while sick with mumps, had "spasms of the left arm," since which time he has had occasional seizures, mostly petit mal, which were controlled to some extent with bromide. Was admitted here April 3.

About three weeks before this had influenza complicated with pneumonia. He seemed to be recovering from this attack when he developed an acute mania, was very restless, sleepless and noisy. Developed delusions directed against his wife and children, etc. Was controlled by drugs before entering the hospital, a considerable amount of morphin being used.

Upon entering the hospital he was noisy, talkative and did not sleep much. It was feared that he would die from exhaustion, but by careful feeding and attention to his general condition he gradually improved, and ultimately made a good recovery from his mania, and left the hospital in his usual state of mind. A letter from him states that he is feeling well and able to attend to some business affairs, but is not trying to do church work. This man had two Wassermann tests, which were reported as 2 plus and 3 plus.

In the case just cited the question of possible neurosyphilis is suggested and left unanswered.

In the following case, taken from our Boston series, there is obviously a combination of hypophrenia, epilepsy, influenza, parturiency and psychosis. Who will say how these should be placed as to cause and effect?

Case 18.—Female, aged twenty-three years, born in Sweden, sixteen years in this country; married; housework.

Family History. This was quite meager. It was believed that her mother was a queer woman, with an exophthalmos, but not definitely psychotic, and no epileptic members of the family, direct or indirect, were known to her husband.

Past History. The patient was always a rather eccentric girl, but with a lovable, happy, sociable disposition, which made her popular in spite of her oddities. Supposedly following a fall "in childhood" (nothing more specific), she began to have convulsive seizures at intervals, persisting until puberty. They then ceased entirely and she is believed to have had none for nearly ten years. However, for some four years or more prior to the present account she had had what may be interpreted as psychic equivalents. "She will clear up for a time and then be peculiar again. . . . She makes simple-minded remarks. . . ."

October 2 the patient developed influenza and three days later was delivered of a seven months' pregnancy. From October 12 to 21 her temperature fluctuated from 97° to 99.5.° About October 20 she began to show mental symptoms. The chief of staff of the hospital wrote: "She now shows fear, anxiety, contriteness for supposed sins, wakefulness and loud calling at night. Wants to climb out of the hospital window, and says she hears and views strangers and has been very bad. Excited, depressed, nervous, feeble-minded (?)."

With this shower of psychic symptoms she began again to have epileptiform convulsions, having two on October 23 and at least one on October 24, the day of admission to the Psychopathic Hospital.

Mental Examination. When the patient was admitted she had a temperature of 101°, pulse of 110, respirations of 40. Examination of lungs confirmed a diagnosis of bronchopneumonia. Thorough mental examination was not practicable, but it was determined that she was approximately oriented, not grossly amnesic, but self-accusatory and deluded in vague and intangible ways. She preserved a fair insight, saying that she had had "influenza and a touch of pneumonia," her mind "mixed up," she was "seeing visions" and her "fits" were coming back, as in childhood, when she "falls down and bites" her tongue. She reacted to visual and auditory hallucinations; she heard the Kaiser outside her room and saw him "with a tail and all black." She was apprehensive and quite amenable to suggestions, obedient and not disorderly. She ate and slept well, kept herself covered and in bed, and was at no time violent.

Course. Her pneumonia signs disappeared by the end of a week and she is believed to have had but one more convulsion. There was at no time any muscular fibrillation, alteration of reflexes, diplopia, exophthalmos, etc., or other evidences of encephalitis.

She was up and about the ward after eight days and made herself agreeable and helpful. A routine mental examination was essentially negative except for absence of insight and a conspicuous defect in memory and intellectual processes, suggestive of hypophrenia. At times she was observed to laugh in a rather silly fashion and at other times to cry a little "for home, husband and family."

Physical examination in all ways negative, except as mentioned. Laboratory findings showed negative urine, blood serum, spinal fluid but positive smear for gonococci.

Psychometric rating was 10.7 on the Yerkes-Bridges point scale, with a variation total of 12. "In the supplementary tests her performance of the construction puzzles was good. She did poorly in the memory tests, adding details not in the original. She coöperated well and was interested."

She was discharged on the twenty-fifth day. The psychotic episode accompanying the convulsion may be interpreted either as a typical delirium, or, as seems better to me, as a transient epileptic psychosis. The basis of hypophrenia seems evident. The seizures are not likely to be regarded as encephalitic in the face of the facts that they preceded the frank pneumonia and were not accompanied by the more typical signs of encephalitis, and there is the history of epilepsy in childhood. The influence of the parturition is more likely to be overestimated than underestimated.

The following history is also from our Boston series, and is more typical of a "pure" epileptic psychosis:

Case 19.—A. T., female, aged twenty-two years, Russian born, German descent: H. W. Admitted November 29, 1918.

Family History. The mother had had epileptic attacks "once every few years." No further data was secured except that she had not been psychotic. Otherwise the family history was irrelevant. Three normal siblings.

Past History. The patient was born in Russia and came to the United States at eighteen. She had always been a healthy child. She had four years of a common school education, and it is reputed that it was difficult for her to learn. She did some work on the farm in Russia, but housework only since arriving in America. "She is a good worker, but does not remain very long in one place, and usually found the work too hard."

Her personality is described as being "always good-natured, sociable and very happy; well liked by people, energetic, fond of dancing and very little of a reader." She used no alcohol, had no court record, was a Lutheran Church member and normally interested therein.

Present Illness. Epilepsy: Began to have epileptiform attacks in January, 1918. They were quite infrequent at first, and in fact there is no positive evidence that she ever had any more than the one first attack until after her influenza.

Influenza. The last of October she contracted influenza and was in the B. Hospital for three weeks. She then returned to her employer's home, but was not permitted to work on account of her physical weakness. November 23 she had a series of epileptic attacks (these are the words of the informant, and unfortunately

no further data was secured, except a corroboration by the patient of the occurrence of some seizures). She was in bed two days following this and incapacitated by weakness for two more days. November 28 "she began to forget things," showed queer conduct, disorder, said "flies kept her awake at night and that people were mean to her, that everyone was about to die, that the sun had gone down and hence her mother had died, everyone said their prayers and appointed her employer as her lawyer and delivered to him all of her small effects."

Hospital Admission. She was very noisy when first admitted, singing at the top of her voice as she marched about the ward gesticulating. The ideas that "race through her mind" were expressed in her endless loud singing, and she was quite inaccessible.

Mental Examination. The patient was totally disoriented in all spheres at times, although at other times gave correctly her name and address and once the date nearly correctly. After the first day she grew more quiet, was for a time depressed and then again disturbed. No delusions or hallucinations were proved. The attention was very poor, associations loose and slow, train of thought frequently broken and revealing irrelevancies. Her memory was notably defective for both recent and remote events.

Later the patient became apparently normal, so remained for a few days, and then became disturbed again within the week. A note reads:

"She is grunting and groaning in a monotonous, noisy way, 'Oh, Oh'-ing and 'Oh, my God'-ing with tireless repetition, not even stopping long enough to define her pains or answer questions. "Here, there, help me, God! In my legs! Oh, my God! Oh, Oh, my arms! Oh, my legs and arms! Oh, my God! Oh, Oh!"

Physical examination wholly negative, including gynecologic. Neurologic examination, including ophthalmoscopic, wholly negative, except for pseudoclonuses on the right side. Laboratory examination of blood, blood serum, spinal fluid and urine were negative.

Course. After ten days' observation she was committed to the Westborough State Hospital. I quote from a letter from the Superintendent, Dr. H. O. Spalding, regarding her condition on June 14, six months after commitment:

"We diagnosed her as a case of epilepsy. Wassermann negative. Orientation impaired. Train of thought confused and retarded. At times shows some spontaneity; emotionally unstable, apprehensive and worried. Hallucinations not established. Insight partial. She has improved some and goes to the industrial room daily and gets along well with the nurses and patients."

The following case from the writer's private practice may be briefly referred to here:

CASE 20.—A male, aged sixty-one years, developed epileptiform manifestations at the age of fifty-four. He was carefully studied by several neurologists, and the diagnosis of idiopathic epilepsy was made by exclusion. He had been having petit mal every few months and grand mal about twice a year, the last attack occurring in December, 1918, during the influenza epidemic. He did not, however, have influenza. Pneumonia of very severe grade in November, 1919, was followed by a postfebrile psychosis which was quite typical in its manifestations, gradually clearing and disappearing within a month. One seizure supervened.

III. EVIDENCE THAT INFLUENZA MAY CAUSE EPILEPSY.

Dr. L. Pierce Clark[12] recently presented in a brief report a case of influenza ushered in by epileptic attacks in a child of two years. The epileptiform seizures continued after the influenza, but were decreasing in frequency and severity. As Dr. Clark claims, this is the first similar case reported from the recent epidemic, but as I have pointed out,[31] in previous epidemics the phenomenon has been noted repeatedly. Leichtenstern in his justly celebrated monograph[13] writes:

". . . Influenza frequently begins in children with an eclamptic seizure, and very rarely in adults with typical epileptiform attacks combined with total unconsciousness and succeed in stupor." He then goes on to consider "those cases in which directly following the influenza attack a typical but chronic epilepsy develops with seizures occurring in short or long intervals . . . (but) . . . . so far as we know of these cases they all, after a longer or shorter time, end in recovery. We know of no recorded case in which permanent epilepsy followed influenza, although the occurrence is not thereby excluded. A case . . . of epilepsia gravissima may be mentioned here. . ." He cites the case of a male of seventeen who began to have typical epileptiform seizures a few weeks after the termination of his influenza, which recurred with increasing frequency until ten to twenty-five attacks daily were experienced. Subsequently a distressing psychosis complicated, or at least dominated the picture, and he was committed, but eventually made a complete recovery.

Leichtenstern then goes on to discuss "many other forms of convulsions and disturbances in movement . . . observed during influenza or thereafter."

Gowers[1] cites 39 cases of epilepsy subsequent to scarlet fever, 12 to measles, 8 to typhoid and "a few" only to influenza. Voisin[19] mentions influenza as producing epilepsy, but does not discuss it. Gelineau,[20] in his treatise on epilepsy, discusses the matter at some length. He concludes that influenza is "capable of giving birth to epilepsy or exercising over it influence of augmentation of number

and severity of attacks." He cites one case of his own: "An English girl, aged eight years, in whom there was apparently recovery following a ligation of the vertebral arteries." He cites 3 cases of Biet's,[21] taken, he says, from Ulliel:

1. Jacksonian epilepsy in a physician of twenty-five with recovery.
2. A "young girl" with two epileptic grandparents who developed typical idiopathic epilepsy.
3. Jacksonian epilepsy in a male of forty-one.

He also refers to the cases of Kraepelin, Mariott and Bidon, and notes that some apparently were influenced favorably and some unfavorably.

Gelineau implies in his discussion that these epilepsies are probably manifestations of miliary cortical hemorrhages. This theory is the more plausible, it seems to the present writer, by virtue of the pathologic demonstrations of miliary hemorrhagic encephalitis in deaths from influenza or after influenza.

Other such cases of epileptiform attacks precipitated by influenza have been reported by Ruhemann,[14] Landgraf,[15] Van Deventer,[16] and Jaccoud.[17 18] Van Deventer[16] cites 3 cases, which might be put in this group. One was an alcoholic male, forty-one, in whom influenza began by an epileptic seizure, followed shortly by another. The second was a man of forty, who, shortly after recovery from influenza, had a severe seizure while standing on the sidewalk. A twenty-two-year-old girl of good heredity, but herself peculiar, and excitable, had a typical epileptic attack at the onset of influenza. In all of these previous epileptic symptoms were denied.

Through the kindness of Prof. Adolph Meyer, of Johns Hopkins Medical School, the writer was permitted to see the following case, at the Phipps Psychiatric Clinic, in Baltimore, an abstract of which was graciously furnished.

Case 21.—G., a farmer, aged thirty-five years, was admitted to the Phipps Psychiatric Hospital on January 9, 1920.

Family History. Entirely negative.

Personal History. Born in West Virginia. Measles and whooping-cough in childhood, otherwise quite healthy. He attended school in the country from six to eighteen years, finishing the eighth grade. He helped work his father's farm after school hours, and from the age of twenty-five he managed the farm alone with success. He was always an even tempered person with little tendency to disagree or argue. Never felt blue or restless. He was inclined to stay to himself; rarely mingled with girls. He had felt under obligations to support his family and was following the custom of the family to avoid marriage until late in life. There is history of autoerotism from twelve to sixteen. Promiscuous sex relations until the present time, about once every few months.

Present Illness. In September, 1918, an attack of influenza kept the patient in bed for three weeks with headache, slight fever and extreme weakness, leaving him still weak and sluggish after convalescence. He undertook the usual duties about the farm in spite of his illness. In attacks coming about every other day he reeled as he walked and frequently had to support himself, and was weak and dizzy. He regained sufficient strength to finish jobs without serious handicap until the following summer, when he began to tire easily, and often was obliged to stop to rest. In August, 1919, there were periods of two or three minutes lapse of consciousness coming once or twice a week, when he suddenly stared into space or busied himself meaninglessly with queer undertakings; "mutters or walks about." At one time, while loading hay, he suddenly dropped the fork and wandered about the fields for three minutes without any recollection of the episode.

He has grown continuously weaker and nervous and more forgetful until he was obliged to stop work altogether in the fall of 1919 and January, 1920. He says: "I just lose my mind. It goes away so quick and comes back the same way. I do not know anything." Never falls or convulses. Brother says preceded by "swallowing."

Somatic Status: The patient presents no indication of systemic disorder other than hyperactive K. K. and A. J., fine tremor of the extended fingers and writing defect. Blood and urine negative. B. P., 124–76.

Mental Status and Course in the Hospital: Mental examination negative. While in the ward he has shown nothing in the way of abnormal behavior or attitude other than an occasional appearance of disinterest. Had seven attacks in January. Nine teeth extracted January 28. Three attacks subsequent week.*

The result of the questionnaire addressed to the superintendents of the hospitals for epileptics indicate that such cases were rare in the recent epidemic. Replies from Dr. O. S. Hubbard, superintendent of the Kansas State Hospital for Epileptics; Dr. H. B. Carriel, superintendent of Dixon (Illinois) State Hospital; Dr. A. S. Priddy, superintendent of the Virginia State Epileptic Colony of Madison Heights; Dr. David F. Weeks, superintendent of the Village for Epileptics at Skillman, New Jersey; Dr. L. V. Guthrie, superintendent of the Huntington State Hospital of West Virginia, and Dr. T. B. Bass, superintendent of the State Epileptic Colony of Abilene, Texas, make a unanimous reply in the negative

* In the hospital he had two attacks of lapses of consciousness. On January 14, 1919, he sprang from his bed; brushed the nurse aside and stalked down the corridor to return immediately in full consciousness without recollection of doing anything out of the way. On the 15th he sat quietly in a chair and mumbled in an undertone several times "get 'em out of here" and made brushing movements with the hands. He then took the bed clothes off the chair, turned the mattress down on another bed and was about to crawl into it when he came to himself. He has never had convulsions, tongue biting, incontinence, or falling spells.

to the question as to the number of cases admitted in which epilepsy was given or considered as a precipitating factor.

One further case is, however, reported by Dr. W. T. Shanahan, of Craig Colony.

CASE 22.—J. O'D., male, aged nineteen years.

Family History. Mother died at forty-four years of influenza. Father living and well, aged forty-two years, a barber, for twenty-five years markedly alcoholic.

Patient is the sixth in line of birth of ten living children. Three girls died in infancy. No history of nervous or mental disorders in family.

Past History. Patient born October 17, 1900; apparently normal birth, nursed by mother. History of convulsions during dentition. No difficulty in learning to walk or talk. Alleged to have had infantile paralysis at two years, followed by hemiplegia. Began school at six years, graduated from public school at fifteen years and attended night school for one year. Had measles at three years, diphtheria at twelve years.

Present Illness. Had severe attack of influenza during the fall of 1918. Following this he had a severe convulsion. His convulsions recurred daily for a short time, when he was free for three or four weeks. After admission to the colony he had a typical grand mal seizure, apparently no aura. Seizures occur both during sleep and waking periods.

At time of admission to the colony he was dirty, and apparently had given no attention to personal cleanliness. Features small, with eyes set close together. Ears small and close to head. Nose narrow and pointed. Many carious teeth, some missing. Palate narrow and high arched. Heart, lungs and abdomen negative. Marked right lateral curvature of spine, compensatory for shortening of the right leg. Flaccid paralysis of right lower extremity with extreme atrophy of muscle. Right thigh circumference, 11 inches; left thigh, 17½ inches; right calf, 7½ inches; left calf, 13 inches; right ankle, 6 inches; left ankle, 8 inches. All reflexes normal except right lower extremity. No Babinski.

Mental Examination: Scored fifty-four points with Yerkes-Bridges point scale. Would not coöperate in various tests.

What attitude shall we take toward these cases of apparent epilepsy which were precipitated by influenza? Shall we turn to Gelineau's attractive theory of miliary cortical hemorrhages as the result of influenza and the cause of epilepsy? All of us have seen cases of cerebral concussion followed by epileptiform attacks* and

* Dr. W. F. Bowen, Topeka, gave me the details of the following case: A boy of sixteen was struck in the head with a batted baseball. He walked to the bleachers and sat down holding his head in his hands for a few minutes and then tried to resume play. About an hour later he fell to the ground unconscious. He was unconscious

it has been demonstrated by McCallum[29] and other pathologists that one of the primary lesions of influenza toxin is an endotheliolytic production of multiple hemorrhages. We have shown[11] that this occurs in the brain as well as elsewhere, and may produce symptoms. Now the question arises as to whether these cases reported may not be those so produced, and if so whether or not they are to be regarded as essential idiopathic epilepsy. Of course, the question perhaps hinges altogether on the meaning and delimitation of the word epilepsy.

The opinions of Dr. E. E. Southard, Dr. Adolph Meyer, Dr. S. E. Jelliffe, Dr. Wm. S. Shanahan and Dr. L. Pierce Clark were solicited as representative of the schools of thought concerning epilepsy in this country. The lamented Southard had given me his idea orally and was to have put it in writing the week of his untimely death. That he probably would have taken the view of an organic causation, *i. e.*, "epileptogenic foci and perhaps tissues favorable to epileptic discharge,"[24] for most syndromes which we call epilepsy, whether produced by an influenzal encephalitis, a syphilitic encephalitis or an idiopathic encephalitis, is apparent from such studies as those done in association with Lucas in 1912,[30] and alone in 1908.[24] The opinions of the other men follow:

Dr. Jelliffe writes:*

"That influenza can produce not only somatic interruption of energy distributing pathways by exudative phenomena or abscess formation, or other typical encephalitic process, is obvious. That such interruptions can result in the epileptic discharge is also obvious and well documented. My own experience has scores of cases and the literature is abundant.

"Furthermore, that reduction in resistance, general functional lowering of distribution capacity, *a la Janet's* 'Niveau Mentale,' can permit the specific reactions called epilepsies to come through is also to me obvious, without any microscopic cellular alterations. Microscopic or chemical alterations with energy carrying capacity reduction lie behind these. These are, I think, equally obvious.

"The whole body as a distributing organism—effectors in their totality—can be seriously hampered by the interference in the coördinating pathways. I see no reason why we should not call them epilepsies if we are fairly definite as to what we can agree upon as to what is subsumed under the symbol. My own notion regarding the nosology is purely pragmatic and I am rather a little dubious as to the prevailing absolutistic nosologic entities."

for twenty-four hours and at that time an exploratory craniotomy was decided upon. The brain was exposed and no single large bleeding discharge was found as expected, but the entire surface of the brain exposed was studded with minute focal hemorrhages. The skull and scalp were closed and the lad made an uneventful recovery, but thereafter suffered from typical attacks of epilepsy. The skull was reopened by other surgeons repeatedly in attempts to remove some point of irritation but without avail.

* From a letter of January 15, 1920.

Dr. Adolph Meyer writes (June 16, 1920):

"I can give you my general conception of the relation of epilepsy and infectious diseases. A large number of infectious febrile disorders and toxic disorders tend to lead to deliria and to convulsions. I am in the habit of connecting deliria with conditions which show also through the presence of edema of the membranes and perhaps also of the brain itself. This same condition is observed in epilepsy. To what extent miliary hemorrhages play a specific role in the production of epilepsy I would not be able to say. I do not, however, consider them essential and specific. In the main I would say it is probable that any cortical damage, either by poison or other injury including arteriosclerosis and circulatory disorders, can be the potential foundation for epileptic attacks.

"I may say that I am very much surprised to see so few of the encephalitis cases of the present epidemic with epileptic attacks. For the role of influenza it might be of value to inquire whether the cases that later developed epilepsy showed any special tendency to delirium or any cerebral involvement during the attack."

Dr. Clark writes:

"As regards the epileptic sequelæ of influenza, I am quite well aware of the fact that the Spanish influenza did aggravate in many instances epilepsies previously existing and in some instances seemed to have renewed attacks in those previously in a state of epileptic arrest.

"I think your criticism was quite true, that the boy was probably predisposed to epilepsy in his backwardness of mental development and probably possessed an irritable and sensitive nervous system upon which the influenza seemed to have acted as a precipitating factor for the attacks. In view of these facts one must say that probably the case is not one of essential epilepsy but rather epileptiform and symptomatic in character and probably the prognosis will be very sound in such a case. But this, I think, only goes to prove that the influenza was really an initiator of the disorder and that it would probably not have been in evidence had it not been for the influenza.

"Singularly enough, Dr. Jelliffe thought also that my article concerned itself with influenza in general, and he believes that the present epidemic is not so dissimilar from ordinary influenza, to which I take great exception, after having seen a good deal of it both in clinics and in my own home. The bibliographic references that you gave to the old forms of influenza are quite pertinent to the disorder as we formerly knew it."

Dr. Shanahan writes (abridged from letter of January, 1920):

"I believe that after influenza, or any other severe infection which, during its course, attacks the central nervous system and damages the organic structure so that permanent change results, one may expect not only a mental deterioration but also some of the phe-

nomena ordinarily called epileptic. Again, of course, there may be but temporary disturbance of function of the brain or other organs of the body having control directly or indirectly of brain functioning, *i. e.*, endocrine glands, etc., and, as a result, epileptiform seizures.

"The degree of keenness of observation, the individual equation, the differing viewpoints, the varying severity of the influenza, the different sections of the country or world, the different years or epidemics, must all be considered. In the earlier epidemics classed as influenzal in nature how many looked for symptoms epileptiform in character?

"Personally I feel, as do many others, that the cause of influenza, be it bacterial or something else, makes itself apparent every winter or at least practically so, varying in intensity.

"In the winter of 1915–1916 we had at the colony a considerable number of cases of what was then called influenza. Several adults had marked delirium, twitching, etc. In some young patients, some not epileptic, there was apparently an encephalitis from the symptoms presented. A boy of four years, who was very fair mentally, developed in January, 1916, a severe illness which after a short time resulted fatally. He had had during practically a year preceding no seizures. With the onset of the illness referred to he had a series of severe convulsions with pulmonary edema, following which he continued in a stupor, practically a coma, occasionally crying out. A right hemiplegia developed. Until death, he had frequently convulsive movements confined to part of the right side and then again on the left side, but no further general convulsions. Lumbar punctures gave a clear fluid with no increase in cell count. He presented a double Babinski and exaggerated reflexes on the right side, pupils reacted normally to light, both fundi congested, right disk slightly blurred. Increased pressure observed when lumbar puncture was made on the seventh day of illness. On the ninth day of illness paralysis of the right side was less marked. No evidence of pneumonia. Babinski still present on both sides. Pupils react to light; no strabismus, but a lateral nystagmus was observed at times. On the eleventh day the patient died, apparently of a terminal pulmonary edema. Diagnosis was *encephalitis following influenzal infection*. Autopsy showed tremendous edema of the brain, so that the surface was misshapen, the convolutions being crowded together so that the sulci were only represented by lines. There was recent hemorrhage on the right side of the cerebellum. Unfortunately a microscopic examination of the brain could not be made.

"In November, 1918, during the influenza epidemic, Harry L. R., aged thirty-one years, who had long been a patient at the colony and was subject to frequent periods of mental excitement, developed a severe influenza, with jaundice and high temperature, dying on the eleventh day. Autopsy performed an hour and a half

after death showed the meninges considerably thickened and very cloudy and of the extreme yellow color. There was some hydrops of the subarachnoid space. The yellow discoloration did not extend into the brain substance. The brain itself was firm without gross lesion. Apparently the edema was not as marked as in the other case cited.

"I mention these two cases as a proof of similar infection during two periods and as evidence that extensive involvement of the brain and its membranes occur, and as a result such permanent structural damage takes place as to bring about disturbance of function, so that it would be very possible for the symptoms of an epilepsy to appear, even in an individual not epileptic."

IV. "The Influence of Epilepsy upon Influenza."

This phrase is of French extraction, being taken bodily from the title of Maillard and Brune's article cited above.[10] Their observation that epileptics were unusually susceptible to influenza was supported by experience in this country. Without entering into the subject in detail we may cite as representative testimony the report of the manager of the State Epileptic Village at Skillman, New Jersey.

"When the first case of influenza occurred the population of the village was 900. There was 422 cases of influenza, with 67 deaths. . . . More than 46 per cent. of the entire population contracted the disease, the case incidence being substantially higher among the epileptic patients than among the employees; 48.9 per cent. in the former against 34.8 per cent. in the latter."

Summary. It appears, then, that insufficient attention has been paid to the influence of influenza, or, for that matter, of any of the acute infections, upon idiopathic epilepsy. Little reference to it can be found in the literature. Such fragmentary treatment as the subject receives here and there is inconclusive. The beneficial effect of acute infections, at least in so far as they inhibit epileptic attacks during the febrile period, is insisted upon by probably the majority of those considering the matter at all. One writer inclines toward a sort of specific differentiation, concluding that this infection increases, this one decreases epileptic manifestations. A few writers are convinced that infections benefit epilepsy permanently, and one even suggests exposure to pneumonia as a possible cure for a preëxistent epilepsy. But nearly all of these writers are strangely silent about the most ubiquitous of all modern epidemic infections, influenza.

For this optimistic impression of the effect of influenza upon epilepsy we find some little support from the recent pandemic. Questionnaires addressed to the superintendents of state hospitals

for epileptics were graciously answered. From these, and from data accumulated at the Boston Psychopathic Hospital and a few other sources, evidence of inhibition of attacks during the febrile period, and of decrease in frequency and perhaps severity of attacks following influenza, was secured. Illustrative figures and cases are cited.

On the contrary, however, we also have evidence, secured from the same sources, that the effect of influenza upon epilepsy may be and probably more often is aggravation. This, it appears, may be demonstrated by a simple increase in the frequency, if not in the severity, of the attacks; it may occur as an alteration in the form of the epileptic attacks; or it may appear in the production of a complicating psychosis. All of these unhappy equations are illustrated above by cases. Statistics would indicate that these deleterious effects of influenza were distinctly more frequent than the beneficial effects.

Nor is the obverse side of the picture yet complete. It appears that an epilepsy, previously manifested but long latent, may be fanned into flame again by influenza, and finally that epilepsy may perhaps be primarily caused by influenza in previously healthy persons. Numerous cases of epileptiform seizures occurring for a while after influenza, but usually ceasing, never to recur, have been reported in past epidemics. From the recent epidemic 3 cases are presented. Various opinions are held as to the significance of this phenomenon.

Of the four actions of influenza upon mental disease, which previous studies have led us to conclude are the usual ones, namely, creation, precipitation, aggravation and amelioration, all are represented in the case of epilepsy. As to "creation" some might quibble, but I believe we are pragmatically justified in assuming that the cases reported by Leichtenstern, Landgraf, Ruhemann, Van Deventer, Jaccoud, Clark, Shanahan and others really represent "epilepsy" produced by influenza, albeit epilepsy with a good prognosis, and, of course, not "idiopathic" epilepsy. We are scarcely justified in rejecting what is apparently typical epilepsy merely because the adjective "idiopathic" is no longer strictly applicable or the termination the conventional one. Presumably they are the product of influenzal neurotoxins and a susceptible brain. The fact that they are apparently reversible in reaction may as well be imputed to a peculiarity in the combination; presumably it is dependent on the type of effector (neurotoxin) rather than the type of receptor (neuron). Reversible reactions are not unfamiliar in the case of other diseases usually regarded as permanent, *e. g.*, Schizophrenia.[22]

Finally, the effect of epilepsy on influenza is the production of a generally lowered resistance, and hence abnormally high morbidity and mortality rates as compared with normal patients.

Conclusions. From a study of pertinent literature and of clinical material afforded by the epidemic of influenza of 1918–1919 the interrelations of influenza and epilepsy may be summarized, in conclusion, as follows:

1. The effect of influenza upon idiopathic epilepsy is not uniform.

2. Beneficial influence is occasionally observed; seizures are perhaps usually absent during the febrile state and in some instances occur with decreased frequency after the acute infection. There are no cases on record in which influenza has induced an entire cessation of epileptic attacks once instituted.

3. Deleterious influence is more frequently observed. This is manifested in various ways.

4. Seizures may occur with increased frequency following influenza, both as compared with short periods and long periods of time prior to the acute infection.

5. The character or type of the seizures may change subsequent to the influenza, in addition to or independent of the increase in frequency.

6. Epilepsies whose manifestations have long lain latent may be incited to renewed activity by the attack of influenza.

7. Psychoses may be precipitated in epileptics by influenza, as in non-epileptics.

8. Epileptiform syndromes which resemble typical idiopathic epilepsy, except that recovery usually occurs shortly, are occasionally evoked by influenza. Probably we should regard these as recoverable or "reversible" types of idiopathic epilepsy, the product of influenza and a (possibly) susceptible brain. Possibly they are manifestations of multiple miliary (encephalitic) hemorrhages.

9. But the majority of epileptic patients who had influenza did not exhibit any alteration in their disease.

10. The effect of "epilepsy on influenza" was observed to be a lowered resistance, and hence increased morbidity and mortality rates (as compared with normal persons).

11. Influenza thus appears to exhibit, in the case of epilepsy, the properties previously demonstrated to be operative in the case of the psychoses associated with influenza: creation, precipitation, aggravation and amelioration.

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REVIEWS.

A Text-book of the Practice of Medicine. By James M. Anders, M.D., Ph.D., LL.D., Professor of Medicine, Graduate School of Medicine, University of Pennsylvania; Consultant Physician to the Jewish Hospital and to the Widener Home for Crippled Children; Officier de l'Instruction Publique. Thoroughly Revised, with the Assistance of John H. Musser, Jr., B.S., M.D., Asst. Professor of Medicine, University of Penna.; Physician to the Philadelphia General Hospital; Physician in Charge of the Medical Dispensary, University of Pennsylvania; Assistant Physician and Chief of Dispensary, Presbyterian Hospital. Pp. 1284; fully illustrated. Philadelphia and London: W. B. Saunders Company.

The previous thirteenth edition of this standard work on medicine had received such a thorough overhauling that we did not think that much could well be done to it in the way of omission, addition or revision. Since this former edition, of course, we have participated in a war and many things have been learned and experienced in the domain of internal medicine. The references and text of this new fourteenth edition give abundant proof that the authors have been on the alert and have conscientiously given the reader the important new material as it has appeared in the literature since the 1917 edition. It would be interesting to discuss the text of the changes as they have been made, but the limitations placed on this review do not permit it.

The section on typhoid fever has been somewhat abridged. The sections on typhus fever, yellow fever, cerebrospinal meningitis, pneumonia, icterohemorrhagic spirochetosis, diabetes mellitus, scurvy, pellagra, pernicious anemia, exophthalmic goiter, focal infection, tuberculosis, mumps, measles, hemolytic jaundice, hemolytic anemia of pregnancy and the puerperium have been well amplified. The subject-material covering hay fever and asthma has been much improved by incorporating further studies of these disorders in their relation to foreign protein.

The chapter on influenza has been rewritten, especially including findings gleaned during the recent pandemic.

New subject-headings include bronchial spirochetosis, streptococcic (hemolytic) pneumonia, trench nephritis, disordered action of the heart, chronic (syphilitic) aortitis, interstitial emphysema

epidemic encephalitis, oxycephaly, methyl alcohol poisoning and botulism.

The arrangement of the book remains, as it has always been, extremely satisfactory. For the student and practitioner it is a good, concise work on the broad field of medicine. The present edition has incorporated in its lines the most recent contributions from the literature, making it a volume well worth while.

T. G. S.

THE ROENTGEN DIAGNOSIS OF DISEASES OF THE ALIMENTARY CANAL. By RUSSEL D. CARMAN, M.D., Head of Section of Roentgenology in the Division of Medicine, Mayo Clinic, and Professor of Roentgenology (Mayo Foundation), Graduate School of Medicine, University of Minnesota. Second edition. thoroughly revised. Pp. 676; 626 original illustrations. Philadelphia and London: W. B. Saunders Company.

IN the second edition of this well-written and very readable book the author gives to the profession at work that stands out preëminently among its kind. It has been brought up to date by a revision of the text and the addition of two new chapters—one on hour-glass stomach and the other a chronological abstract of the published work on pneumoperitoneal diagnosis.

While the author has drawn freely on the experience of other workers in like fields, his book, with the exception of the chapter on pneumoperitoneal diagnosis, is largely the result of his own indefatigable efforts. His deductions are based on the observation of many thousands of cases examined by himself and seeing his results checked up at the operating table or in the autopsy room.

The principal feature which distinguishes the second from the first edition is the chapter on hour-glass stomach. This chapter is done with the same thoroughness that characterizes the work on the other chapters. Congenital, acquired and pseudo-hour-glass contractions are discussed, with particular emphasis, on the differentiation of the organic from the spasmodic form of the acquired variety. The chapter on pneumoperitoneum is a reflection of the work done by other investigators, with a description of the technic and a timely warning as to the dangers and complications of this procedure. What the author thinks of it is best told in his own words. "If the patients are carefully chosen pneumoperitoneum should prove a valuable aid to diagnosis, but it should be resorted to only after all other methods of examination have failed."

Distinguishing features of the book are the very good illustrations and complete case reports. It can be heartily recommended as a text-book for the roentgenologist, be his experience large or small.

J. D. Z.

SURGERY OF THE LUNG AND PLEURA. By H. MORRISTON DAVIES, M.A., M.D., M.C. (CANTAB.), F.R.C.S. (ENG.), Hon. Captain, R.A.M.C. (T.), Consulting Surgeon, University College Hospital; Consulting Surgeon, City of London Hospital for Diseases of the Chest; Medical Superintendent, Vale of Clwyd Sanatorium. Pp. 259. New York: Paul Hoeber.

THERE is no doubt a place in our literature for a work dealing with the above subject. It comes close on the heels of several of the very excellent contributions, but written as it is in such an easy and simple style it will no doubt receive a warm reception. Thoracic surgery has improved so remarkably in its ramifications and its technic that we should welcome Davies's experience. The anatomy of the chest is minutely discussed, especially as regards surgical anatomy. The illustrations in this chapter do not do justice to the work either in clearness or in numbers. Intrapleural pressures are discussed in several intensely interesting pages. It is to be regretted that the author does not refer to the vast amount of literature which Evarts Graham has contributed to this subject. The chief shortcoming of the book is the terseness with which empyema is discussed. Barely thirteen pages are devoted to this most important subject. The author differs in his conception of the treatment of streptococcic and pneumococcic empyemas from the view held here in America. Setting up exercises and high caloric feeding in the postoperative management of these cases is not even mentioned. The most valuable portion of the book is the minute description of the surgery of tuberculosis. The subject is extensively discussed, especially as regards nitrogen displacement in various pulmonary tuberculous pathologies and complications. This chapter is the author's best contribution, and it alone will fully compensate the reader of the book. The roentgen-ray pictures are numerous and clear. They show contrasts and hilus pictures with an exactness not often to be found in text-books.

I. S. R.

A LABORATORY MANUAL AND TEXT-BOOK OF EMBRYOLOGY. By CHARLES WILLIAM PRENTISS, Late Professor of Microscopic Anatomy, Northwestern University Medical School, Chicago. Revised and Rewritten by LESLIE BRAINERD AREY, Professor of Microscopic Anatomy at the Northwestern University Medical School. Third edition, enlarged. Pp. 391; 388 illustrations, many in colors. Philadelphia and London: W. B. Saunders Company.

THE fundamental importance of a thorough knowledge of the stages by which the organs of men have reached their adult develop-

ment becomes more and more apparent to abdominal surgeons and other specialists as cases of anomalous formations and congenital malformations of various structures are met and studied. Considered from a purely scientific aspect, obstetrics is essentially but applied embryology. To the student, embryology is in itself, perhaps, a dry and quickly forgotten subject; but the contrasting of the evolution of the human organs with those of other vertebrates and the relation of these steps to the gross anatomy of the organs, as is done in this volume, brings out a new interest. To these two classes, students and practitioners, the present volume must appeal. The book is well printed, the illustrations not too complex, well executed, and the book is enhanced by many colored plates.

The subject-matter is divided into various chapters devoted to studies of the germ cells, the germ layer, chick, human and pig embryos and their dissections. The various basic systems of the body are then taken up and fully described as to the various changes and modifications which occur in them during their development to adult organs.

That the book has gone through three editions in five years is a token of its value and of its appreciation by the medical profession.

P. F. W.

NERVOUS AND MENTAL DISEASES. By ARCHIBALD CHURCH, M.D., Professor of Nervous and Mental Diseases in the Northwestern University Medical School, Chicago, and FREDERICK PETERSON, M.D., formerly Professor of Psychiatry, Columbia University. Ninth edition, revised. Pp. 949; 350 illustrations. Philadelphia and London: W. B. Saunders Company.

THE ninth edition of this work on *Nervous and Mental Diseases* by Church and Peterson shows little radical change from the edition published in 1915.

The book is divided, as heretofore, into two separate treatises. The first is by Church and deals with nervous diseases, while the second, by Peterson, is devoted exclusively to mental disorders.

It is interesting to note in both sections that only passing reference is paid to the theories and studies of Freud. The authors remark: "Some radical views which have attained considerable popularity have not been incorporated, more time and experience being thought requisite for their unquestioned establishment." Likewise only scant treatment is given to the field of the war neuroses, concerning which so much has been recently in print.

The only chapters which show any active reconstruction are those on general paralysis of the insane and traumatic insanity, these being elaborated and corrected in view of the advances made in the etiology and treatment of these disorders.

The book is an excellent text on the subject for general practitioners, and especially for students, as it is conservative and concise, and all the subjects are presented in a systematic and interesting manner. The new edition will undoubtedly continue the excellent reputation of its predecessors. F. H. L.

SLEEP-WALKING AND MOON-WALKING. A MEDICO-LITERARY STUDY. By DR. J. SODGER, Vienna. Translated by LOUISE BRINK. From the Nervous and Mental Disease Monograph Series, No. 31. Pp. 138. New York and Washington.

THIS psychoanalytic monograph is perhaps best described by quoting from the first and the last chapters of the edition.

"Psychoanalysis holds a key to the problem of sleep-walking, which alone has been able to unlock the mysteries of its causes and its significance. This key is the principle of wish fulfilment."

"Sleep-walking under or without the influence of the moon represents a motor outbreak of the unconscious, and serves, like the dream, the fulfilment of secret forbidden wishes, first of the present, behind which, however, infantile wishes regularly hide. Both prove themselves in all the cases analyzed more or less completely of a sexual erotic nature."

The above phrases describe the monograph *in toto*.

F. H. L.

DISEASES OF THE EAR. By PHILIP D. KERRISON, M.D., Aural Surgeon to the Willard Parker Hospital for Infectious Diseases. Second edition. Pp. 596; 333 illustrations. Philadelphia: J. B. Lippincott Company, 1921.

THE second edition of Kerrison's book fully conforms to the high standard set by the previous edition and should continue its popularity. The arrangement of the subject-matter is unique, and, on the whole, praiseworthy, making for ease of reference while adding to the conciseness and attractiveness of the text. The cuts are original and well drawn, admirably illustrating the subject-matter. Naturally, from the nature of the case, most of them are anatomical and give the student new and often illuminating ideas as to the topographical anatomy of the temporal bone in its relation to aural function and operative procedures. New chapters have been added and old ones amplified to include the latest developments in aural research and technic. Such, for instance, is the comment on postoperative tissue repair in mastoid surgery, and the resultant modification in postoperative technic

in the closure and treatment of the mastoid wound, resulting in quicker and more satisfactory results in healing. The result of the study of the cerebrospinal fluid in various diseases is given and its influence in correcting errors of diagnosis in meningeal lesions and disorders of otitic origin is interpreted. The first edition devoted considerably more space to the labyrinth in disease and the various tests of its function than most text-books on otology. This work is now carried forward by the addition of a short chapter on Bárány's theory of cerebellar localization, a subject very much before the otological and neurological branches of the profession at the present time.

The volume is a complete work on ear diseases and gives the reader a most satisfactory and up-to-date review of the subject as well as a definite and detailed guide to the various therapeutical and surgical procedures indicated in different aural conditions.

G. M. C.

VENEREAL DISEASES. THEIR CLINICAL ASPECT AND TREATMENT. By J. E. R. McDONAGH, F.R.C.S., London Lock Hospital. First edition. Pp. 403; 127 illustrations (106 in color). St. Louis: C. V. Mosby Company.

THE following statements are to be found in this volume on venereal diseases.

Page 5: "As the following pages will indicate, I believe that the Spirocheta pallida is only the adult male of a coccidial protozoön . . . As proofs for these views are beyond the scope of this, a clinical volume, and as the work is being confirmed, a special pathological volume will be published as soon as possible."

Page 13: "There is only one certain way of diagnosticating a sore, and that is by looking at it."

Page 16: "If a patient has a sore or sores on the skin of his penis the chances are 90 to 1 that they are syphilitic."

Page 14: "Connective-tissue cells can proliferate more abundantly in some areas than in others; moreover, there are areas in which, even if the connective-tissue cells did proliferate abundantly, it would be difficult to feel them."

Page 32: "The distribution of the blood supply in the skin is not unlike that in the liver, *i. e.*, the skin is divided into circular areas roughly about the size of a shilling. . . . In the center of each circular area an artery runs. . . . It is along this central artery that the organisms reach the skin and it is in the walls of vessels that the organisms develop. . . . Occlusion of the lumen would result in the loss of blood supply to the circular area affected; consequently, the skin corresponding to this area would necrose, an ulcer would be formed, or, in other words, a gumma."

Page 42: "Syphilitic lymphatic glands are hard and discrete, or enlarged, matted together and soft."

Page 274: "The gonococcus is not necessarily a pus-producing organism; note how comparatively infrequently gonorrheal complications are associated with pus formation."

Page 276: "It is probably owing to their difference of tissue in the two parts of the canal that strictures are most apt to develop in the posterior part of the urethra."

Page 296: "If the gland is enormously enlarged and painful and the two lobes cannot be differentiated the patient if under fifty years of age has a prostatic abscess."

Page 297 (speaking of prostatic comma shreds): "Their presence usually denotes that the patient is either neurasthenic or has been overtreated."

Page 298 (speaking of complete urinary retention in acute posterior gonorrheal urethritis): "In no condition is the effect of colloidal manganese more marked, because one injection will rid the patient of the subjective symptoms and enable him to pass his urine without assistance."

Page 387: "It is my object, therefore, in this chapter to attempt to show the relationship between syphilis and other diseases; but particularly between the symptoms produced by it and well-known poisons, and the role it plays in the etiology of malignant disease."

Anyone subscribing to these tenets will be interested in possessing this book. A. R.

THE STORY OF THE AMERICAN RED CROSS IN ITALY. By CHARLES M. BAKEWELL. Pp. 208; 21 illustrations. New York: The Macmillan Company.

AN account of the American Red Cross activities in behalf of the Italian army, of the American soldiers who served in Italy, and of the suffering population throughout the country during and after the World War, is interwoven with observations on the political situation, war history and descriptive passages. Emphasis is laid on the improved morale of the Italian people and the better feeling toward America due directly to Red Cross relief work. Many grateful expressions from Italians are cited. Chapters entitled "A Tour through Italy in the Wake of the Red Cross" comment on conditions in principal Italian cities and resemble a guide book in pointing out interesting places. The fight against tuberculosis and the organized continuation of the work through the League of Red Cross Societies are featured in the conclusion. There are maps, pictures, and appendices giving an account to expenditures and list of personnel. T. G. M.

PROGRESS
OF
MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

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Uremia, (Harvey Lecture, 1920.) — FOSTER (*Jour. Am. Med. Assn.*, 1921, lxxvi, 281) says our present-day conception of uremia is reviewed and summarized. It is noted that uremia is an intoxication which may occur in nephritis and which manifests itself by psychomotor disturbances. The symptoms may be roughly divided into three groups: (1) Toxic: headache, vomiting, diarrhea, amaurosis; (2) psychic: hallucinatory paranoid states, stupor and coma; (3) motor: transient paralyses, paresis and hemiplegia and convulsions. Dependent upon the occurrence of these symptoms in a given case clinical types of uremia are recognized: (1) Convulsive or epileptiform type. Initiated by headache and sudden amaurosis (the latter without demonstrable lesions in the eye), a convulsion occurs. Coma is a sequel. The convulsive seizures and the not infrequent recovery are striking features. (2) A second type characterized by gradually deepening coma without psychic or motor disturbances. (3) A third type in which lethargy and somnolence occur along with gastro-intestinal and psychic disorders. Visual disturbances occur, as a rule, only in the presence of demonstrable retinal changes (hemorrhages, exudate, neuritis). Convulsions are absent. Edema of the brain in connection with uremia is discussed and the author finds that "in its highest severity it occurs with constancy in but one type of uremia, that type in which stupor and coma without convulsion, without psychic or motor disorders, is the prominent nervous symptom." Definite cerebral hyperemia, with or without slight edema, he has observed in only one group of cases, viz., that in which the subject had died of the convulsive type of uremia. Having

previously noted that, anatomically, "aside from the lesions in the kidney and occasionally ulceration in the gastro-intestinal tract uremia leaves but few signs," and having discussed the cerebral condition frequently found in association with certain types of the condition, the author considers uremia from the standpoint of an intoxication. Anuria (as a result of ureteral obstruction, ligation of renal arteries, bilateral nephrectomy, etc.) is discussed and the symptoms resulting from it differentiated from those occurring in epileptiform uremia. Other differences are pointed out: The retention of water in the case of the anuria with the resulting dilution in the body of the retained nitrogenous substances; in anuria all the substances normally excreted in the body are held back while in nephritis some are retained more than others. It is pointed out that uremia may not be only a consequence of water loss through the kidneys but may also follow diaphoresis or restriction of the fluid intake. In connection with his discussion of the blood chemistry of uremia the author states that it seems definite that the tissues retain more of the nitrogenous bodies than does the blood and that there is some ground for the belief that the excess of these bodies in the blood is simply an expression of the supersaturation of the tissues. The sharp, clinical contrast between the convulsive and asthenic types of uremia is emphasized. Feeling that if the former is an intoxication the toxin should be recoverable from the blood or tissues the author attempted the isolation of various organic substances from the blood of patients suffering from convulsive uremia in order to study their effect on animals. Colloidal methods such as used for the separation of alkaloidal bases were employed and the base recovered in a pure state for the tests. The solution of the base from the blood of 22 cases of convulsive uremia, and from twice that number of controls, was injected intraperitoneally into guinea-pigs. In the case of the former uniformly fatal results were obtained. Polypnea, muscular twitching, convulsive seizures and death within a few minutes was the usual occurrence. In some experiments paresis of the hind legs and diarrhea preceded the convulsions. In a few convulsions were absent, death being preceded by twitching movements and a stuporous condition. No toxic substance was isolated from the blood of control patients. The substance isolated is basic in its properties and forms crystalline salts with platinum and gold. Nothing is known of its chemical nature because of the inability to collect a sufficient quantity for analysis. Although the author states that "the existence of a toxin in uremic blood will not have been demonstrated until its chemical identity is known," he feels that his investigations "seem to indicate that the blood of patients with epileptiform uremia contains an organic base which is toxic."

A Study of the Spinal Fluid in 1869 Cases of Syphilis in All Stages.—WILE and MARSHALL (*Arch. Dermatol. and Syphil.*, 1921, iii, 293). Based on a study of these cases the authors conclude: (1) The nervous system, if uninvolved as shown by the accepted criteria during the first months of the infection, is seldom involved later. A negative preliminary puncture followed by positive findings at a later date occurred in only three of several thousand cases punctured. (2) Of the several criteria indicating involvement, the increase of organic solids

is found to be slightly higher than either the cell count or Wassermann reaction, the relative value being indicated in the order just mentioned. (3) A considerable degree of cerebrospinal involvement may be present in the latent period of syphilis without manifesting any signs or symptoms. (4) Such asymptomatic cases may become symptomatic later, and a study of the colloidal gold curve in these cases is of some value in estimating the ultimate prognosis of the case. (5) Comparing the large number of cases of primary and secondary syphilis in which positive findings are found with the relatively small percentage of late neurosyphilis as compared to total syphilitic incidence, we must conclude that a large number of early cases are in the nature of a meningeal roseola which is transitory in its clinical aspects. (6) The interpretation of the lumbar puncture findings particularly early in the incidence of the disease, constitutes a valuable guide in estimating the ultimate prognosis of the disease with regard to the integrity of the nervous system.

Industrial Lead Poisoning.—SHIE (*Jour. Am. Med. Assn.*, 1921, lxxvi, 835). Basing his opinions on findings encountered in a study of a large series of cases the author feels that certain symptoms have been unduly emphasized in the diagnosis of plumbism. Anemia is rare. Pallor of the skin is common, possibly due to peripheral vasoconstriction. Basophilia is unfrequent in acute cases and rare in chronic cases. The occurrence of hypertension is variable; it was practically absent in cases of plumbism occurring in pottery workers, whereas among "lead refiners" exposed to fumes it is almost universally present. Perhaps the difference in the form of lead to which the workers were exposed is responsible. Constipation is usual, though by no means constant. Diarrhea was a frequent complaint. A point of diagnostic value is the finding of an increased mononuclear percentage in the differential white blood cell count. This was almost invariably present. A lead line was noted in 90 per cent. of the cases. Peripheral nerve palsies were common. The importance of prophylactic measures (improved working conditions, personal hygiene, medical supervision of industries in which the lead hazard is present) is emphasized.

Serious Reactions to Repeated Transfusions in Pernicious Anemia.—BOWCOCK (*Johns Hopkins Hosp. Bull.*, 1921, xxxii, 83). From a review of the literature and careful study of three cases at the Johns Hopkins Hospital in which after a large number of transfusions there occurred extremely severe reactions following the transfusion of apparently compatible blood the author arrives at the following conclusions: "(1) In certain patients suffering with pernicious anemia who have been transfused repeatedly transfusion becomes self-limited because of the inadequacy of methods for selecting suitable donors. (2) The difficulty having once been discovered no attempt should be made to transfuse these patients. (3) The severe reaction is probably due to an antiphylactic manifestation, and not to hemolysis *per se*. (4) Blood-matching should be carried out with the greatest care, whenever possible the incubation period should be at least two hours, or longer. (5) Blood serum free from cellular elements may produce bone-marrow stimulation. (6) Members of Group IV cannot be regarded absolutely as universal donors."

SURGERY

UNDER THE CHARGE OF

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Hypophyseal Duct Tumors.—DUFFY (*Annals of Surgery*, 1920, lxxii, 532 and 725) says, in concluding a very excellent article on this subject, although there are embryological possibilities for growth of squamous epithelial neoplasms between the pharynx and the sella turcica, the great majority of such tumors develop from squamous epithelial embryonic rests of the hypophyseal duct either in the infundibulum or beneath the upper surface of the anterior lobe of the hypophysis. Of either origin the tumor usually presents above the sella. In view of the fact that a majority of these tumors are suprasellar in position from the beginning and that nearly all early assume this position, it appears that they are especially suitable surgically for an intracranial approach. In tumors which arise beneath the capsule of the anterior lobe the latter becomes flattened out below and a transsphenoidal approach may destroy the entire anterior lobe of the hypophysis. The tumors derived from embryological remnants of the hypophyseal duct are quite different in structure from those derived from Rathke's pouch or cleft (between the anterior and posterior hypophyseal lobes). From the duct reliqui develop papillary squamous epithelial adamantinomatous tumors; whereas, from Rathke's pouch or the cleft develop simpler cysts lined by a single layer of ciliated cylindrical epithelium. The hypophyseal duct tumors histologically may be divided into three groups. Group I is that of the papillary cyst or intracystic papilloma which is histologically the most benign example of hypophyseal duct tumors. Group II includes the uncalcified or calcified adamantinomas (solid or cystic), the rarer tumors which closely resemble the basal epithelioma of skin, and the more complicated adamantinomas, the "autochthonous teratomas" of Ewing. The tumors of this group may show criteria of local malignancy, but do not metastasize. Group III comprises a very rare group of cases which show all the earmarks of malignant spinal-cell carcinoma and may metastasize extensively to the cervical lymphatics. The frequent occurrence of calcification in hypophyseal duct tumors is an important diagnostic fact. At variance with the statement of Jackson (1916) that roentgenography is usually negative, in each adamantinomatous tumor described by the writer the roentgenogram shows a suprasellar calcified nodule. The rarity of such calcified shadows in tumors of other types (adenomas, endotheliomas, etc.) makes such nodular shadows almost pathognomonic. The occurrence of bone in hypophyseal duct adamantinomas is not due to the presence of a congenital osseous anlage but is a result of activity on the part of the stroma,

apparently excited by the presence of calcium salts which have been deposited in the necrotic stratified epithelium. The mechanism of osseous change is apparently similar to that described by Nicholson for the same phenomenon in calcified cutaneous epitheliomas. Hypophyseal duct tumors of the infundibulum not infrequently break into the third ventricle. To the contrary, the tumors of the ependyma or choroid plexus of the third ventricle are very rarely present in the suprasellar region; this is explained by spread of the growth along the intraventricular paths of least resistance. During operations on suprasellar cysts in intimate contact with the floor of the third ventricle microscopic demonstration of squamous epithelium from the lining of the cyst will assure the surgeon that the cyst (or solid tumor) originated below the ventricle. A pathological fact of importance for the surgeon to appreciate is the intimate and delicate relation of such cysts with the floor of the ventricle, from which they are frequently separated only by a very thin membrane. The very frequent occurrence of the clinical syndrome of dystrophia adiposogenitalis (Frölich) in patients suffering with hypophyseal duct (squamous epithelial) tumors makes the pathological findings in the genital organs of two individuals of particular interest. In the uterus of a twenty-year-old girl there was an atrophic endometrium, almost equal to that of the senile type, associated with cessation of the process of ovulation (ovaries). The testes of a thirty-five-year-oid man showed a marked atrophy of the spermatogenous epithelium.

Management of the Cervical Stump and the Round and Broad Ligaments when Performing Supravaginal Hysterectomy.—Bissel (*Surg., Gynec. and Obst.*, 1920, xxxi, vi, 578), says if the action of the round ligaments, when these ligaments are anchored to the cervical stump, effects a change in the position of the cervix, then this change of position must be toward the symphysis and from the coccyx, and as the normal position of the cervix is in the immediate region of the coccyx, any marked change of its position toward the symphysis constitutes a displacement. If, when the round ligaments are anchored to the normally posed cervix, the position of the cervix after operation is found maintained, it is proof that the anchored round ligaments have had no influence upon the position of the cervix, as the direction of this influence, if any, must be toward the symphysis. A normal fascial diaphragm independently maintains the cervix in a normal position. Its action is constant and its resistance greater than that of the round ligaments, so that the influence of the anchored round ligaments upon the cervix must be *nil* when the fascial pelvic diaphragm is normal. If the posterior area of the fascial diaphragm is stretched by a retroposed corpus or tumor in the cul-de-sac of Douglas so as to advance the cervix toward the symphysis, shortening of the uterosacral or posterior ligaments is a more logical procedure than anchoring of the round ligaments to the cervical stump. If the entire fascial diaphragm has been injured sufficiently to permit of the cervix advancing and descending toward the vulva and an intra-abdominal removal of the corpus is deemed advisable, then the corpus should be removed without reference to the position of the cervix and the prolapse of the cervix with the vaginal vault corrected subsequently by lapping the fascia of the anterior vagi-

nal wall. No adequate proof has yet been offered to show that the influence of the round ligaments, when anchored to the cervix, enters as a factor, in the slightest degree, in maintaining the normal position of the cervix nor in restoring a displaced cervix to normal. Prolapse of the cervix does not and cannot occur after supravaginal hysterectomy, if previous to the operation the fascial diaphragm is uninjured and the cervix is in normal position.

Renal Hematuria as a Symptom of a Perinephritic Condition of the Kidneys.—YOUNG (*Surg., Gynec. and Obst.*, 1920, xxxi, 478) says that of 1300 cases treated in the house service of the Genito-urinary Department of the Massachusetts General Hospital, 40 per cent. had a history of gross hematuria at some time or other in the history of the disease. The cause of renal hematuria can be demonstrated in all but a very small proportion of cases. Kidney bleeding of unknown origin has been known to be enough to threaten life and require nephrectomy. A horseshoe kidney, a slightly movable kidney, a varix of a renal papilla may occasionally exist without the possibility of positive preoperative diagnosis. In a few instances the split function may show considerable damage on the bleeding side and the pyelogram a considerable deviation from the normal, a combination which should require exploration; but these cases are very rare and operation as a routine exploratory procedure in cases of hematuria of unknown origin is unwise, as there is no assurance that it will have any effect on the progress of the bleeding. In a fair number of these cases a nephritis has been proved to be the cause of trouble. It is reasonable to believe that in a majority of these cases there is an early unrecognized nephritis or a perinephritic condition which can be, and probably often is, the cause of hematuria, and that this condition may or may not go on to a progressive damage of the kidney, depending on conditions which we do not as yet understand. In certain of these cases the primary focus of damage can be recognized, and when eliminated will prevent the later development of the disease.

Blastomycosis.—MOORE (*Surg., Gynec. and Obst.*, 1920, xxxi, 590) reports a case of cranial blastomycotic infection. Little is to be found in our modern text-books on the systemic involvement of various organs of the body by this infection. Moore's case received the infection through a puncture wound as many of the cases do. The infection in this case was probably introduced through the mouth from the splinters habitually carried in the mouth. The treatment of the case was hardly radical enough in destroying the various recurring foci of the disease. The eye should have been sacrificed earlier, and radium used in the orbit as the roentgen ray was apparently the best agent used in the treating of the lesions on the face and neck. The disease remained more or less local for a long time notwithstanding its tendency to spread through the lymphatics and become systemic. No organisms were obtained either from the urine or sputum, nor did we succeed in getting a culture from the blood. The infection of the brain was possibly through the ophthalmic vein or through the veins of the scalp

and emissary vein through the skull. The study of the organisms in the different lesions and tissues showed a considerable variation in their size; those from the abscesses of the face, neck, and orbit, showing the large forms, while no large forms could be found either in the pus or the tissue from the brain. There are many budding forms of the organisms, but no evidence of endosporulation, as in coccidiodes.

PEDIATRICS

UNDER THE CHARGE OF
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A Clinical Classification of Diarrheas.—ROYSTER (*Arch. Ped.* September, 1920) classifies the diarrheas of early life as follows: Food injury (acute) from overloading the digestive tract, particularly the stomach, with proper food; the accidental administration of an excess of one or more food elements in a bottle baby's formula, either fat, carbohydrate or protein nervous diarrhea from sudden overheating or sudden chilling, excitement or fear, improper or indigestible food; food injury (chronic) from the habitual administration of too large quantities of one or more of the normal and proper food elements or mixtures too strong in all elements; fermental diarrhea; infectious diarrheas due to the dysentery group of organisms, the gas bacillus or other organisms. An effort was made to ascertain what relation existed between the onset of summer diarrhea and the temperature and humidity. Last summer the warm weather was late, its onset not having been well established before June 12, which was two or three weeks later than usual. The incidence of diarrhea was correspondingly late in its appearance. The mean of the observations of the local weather was taken as the only practical record. The temperature was averaged each day from the highest to the lowest. The relative humidity was observed at 8 A.M. and 8 P.M., and an average taken. The incidence of cases exactly followed these curves. It was of great interest to note the height of the incidence on the day following the height of the temperature.

Effort Syndrome in Children.—KERLEY (*Arch. Ped.*, August, 1920) reports several cases which are given as illustrations of the condition to which this name is applied. As the most prominent symptoms involve the circulatory and nervous systems, it has also been called "neurocirculatory asthenia" or "neurocirculatory myasthenia." The chief cause has been found to be infections from the tonsils, teeth and other foci. The child who may later become a member of this group presents a typical history, which tells of absence of capacity for sus-

tained effort either mental or physical. They are usually backward in school although they are intelligent, but seem unable to apply themselves sufficiently to keep up with the average. They are also physically unfit for the usual activities of childhood. They tire readily and prefer to be spectators rather than to participate actively in the games and amusements. They are not ill and usually it is impossible to show evidence of disease even under the most careful and rigid examination. One of the distinguishing characteristics is lack of nervous control. Therapeutically the results have been discouraging. They do fairly well in non-strenuous occupations. It is unusual to find children of this type the offspring of vigorous young persons. In a great majority of cases they are the offspring of a weakly mother with little resistance and of lessened endurance capacity. A strong vigorous mother will do much to offset the unfavorable influence on the progeny of a weakly male. The progeny of vigorous males is greatly handicapped by an inferior mother.

Bodily Mechanics.—Talbot and Brown (*Am. Jour. Dis. Children*, September, 1920) report a number of cases of cyclic vomiting and other obscure intestinal conditions as the result of poor posture. They think that faulty bodily mechanics was responsible for a great loss of efficiency among adults during the war. Correcting it changed inefficient men into efficient soldiers. It is a condition common to all ages, and it is surprisingly prevalent. It is easily corrected and can be most economically done during childhood. It is responsible for most instances of diminished power of digesting fats in children. It is the cause for a certain amount of chronic constipation. It is the background and probably the cause of many, if not of most, of the cases of recurrent vomiting. In many instances the symptoms of acute abdominal pain in children, when associated with chronic constipation, is due to poor bodily mechanics. These symptoms are often so severe that they are confused with those of acute intestinal obstruction due to other causes. In the cases reported, in which the faulty postures have been corrected in conjunction with other treatment, the patients have shown a more speedy recovery than in cases without correction.

The Schick Test, Its Control, and Active Immunization Against Diphtheria—Blau (*New York Med. Jour.*, August 28, 1920) in his work used the capillary outfit as furnished by the New York Health Department. The technic is as follows: Break off one end of the capillary tube not having the black mark. Push the broken end through the neck of the rubber bulb until it punctures the diaphragm and enters the cavity of the bulb. Break off the other end of the tube. Expel the contents into one of the vials containing 10 c.c. of saline solution by placing the index finger over the opening in the larger end of the bulb. Rinse the capillary tube by drawing up saline solution several times. Cork the saline vial and shake the dilution. Inject 0.2 c.c. of the diluted toxin, representing one-fiftieth minimum lethal dose for the guinea-pig, intracutaneously on the flexor surface of the left forearm. The control test is proceeded with in the same manner using the capillary tube with the black mark, and making the injection into the flexor surface of the right forearm. The reactions should be observed at the

end of twenty-four and forty-eight hours, basing the final judgment upon the last reading. The positive reading becomes apparent at the end of from one to four days, averaging at the end of the second day, at a time when the pseudo-element of the reaction has disappeared. It consists of a definitely circumscribed area of redness, from 1 to 2½ cm. in diameter, with a superficial scaling and a beginning brownish pigmentation. A strongly positive reaction will occasionally show vesiculation of the surface layers of the epithelium. The reaction gradually disappears in from one to four weeks going through various stages of scaling and pigmentation. After about two weeks a distinct brownish area is seen at the site of the injection. Occasionally a pseudo-reaction is manifested. This shows an indefinite area of redness of varying size, surrounded by a secondary areolar which shades into the surrounding skin. The pseudo-reaction appears earlier than the positive reaction in from six to eighteen hours, reaches its height in from twenty-four to thirty-six hours, and disappears by the end of from two to four days, at the time when the positive reaction becomes apparent, and may have a poorly defined area of pigmentation but no scaling. The combined reaction shows a positive and a pseudo-reaction in one. The positive element of the reaction becomes apparent at the end of from two to four days, at a time when the pseudo-reaction has disappeared. The appearance of the positive element is the same as the positive uncombined reaction. The appearance of the pseudo-reaction is the same as the uncombined pseudo-reaction, and resembles the reading at the site of the control test if there is a reaction at the control, with which it should be compared. The doubtful reaction is where the reaction is not typically positive negative, nor a pseudo-reaction. In these cases the reading should be made as positive. In the control reaction nothing is seen, but occasionally it shows a pseudo-reaction. The Schick test is positive between the ages of one and four years in about 32 per cent. of normal children. It is positive in a slightly larger proportion of measles cases, in twice as many scarlet fever cases, and in nearly three times as many cases of poliomyelitis. After the sixth year the proportion of positive reactions rapidly decreases, being positive in about 10 per cent. In adults 85 to 95 per cent. of the tests are negative. For active immunization a solution of undiluted toxin and antitoxin is used.

The Dietetic Treatment of Summer Diarrhea.—GRIFFITH (*Arch. Ped.*, August, 1920) says that the correct management of the diet is the most important factor in treatment. The first and the most important step is the immediate and complete withdrawal of food at the beginning of the attack. It is advisable to instruct mothers that with any digestive disturbance whatever, food should be withdrawn without waiting to call the doctor. The second step is the removal of any food already in the intestines. Castor oil or magnesia are advised to accomplish this. If there is vomiting, it may be necessary to wait for its subsidence before giving the purgative. A large intestinal douche can, however, be given at once. The length of the period of starvation depends upon the case. A breast-fed baby may be kept from suckling for twenty-four hours. Bottle-fed babies usually require a longer time. Water should be given freely, and it is often a great relief to the mind of the mother, if she is allowed to use barley water. So long as the fever remains

showing that an infection is still present, resumption of the milk diet should be delayed. When it is started, it should be given in small quantities diluted and preferably skimmed, and the return to the original strength should be made gradually. An excess of fat or sugar may cause diarrhea. Broths thickened with starchy substances or even thick porridges are of great value when the time for the return to food has come and the action of the milk is feared. In obstinate cases it is sometimes best to abandon the milk mixture and to use whey, casein milk, buttermilk, or the like. The thick gruels are very valuable as foods. On account of the starch, it is not advisable to continue their use over long periods. On account of the danger of relapse and recurrence restriction of the diet should be continued for the duration of hot weather. Gain of weight in these cases becomes of minor importance for the time. Acidosis is one of the great dangers during diarrhea.

OBSTETRICS

UNDER THE CHARGE OF

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The Prophylactic Forceps Operation.—DeLee (*Am. Jour. Obst.*, October, 1920, No. 1) contributes a paper in which he urges that many patients be delivered by the use of forceps without waiting for spontaneous expulsion. His method is as follows: When the pains are well established and cervix partly dilated, morphin-scopolamin are given and $\frac{1}{400}$ scopolamin given several times afterward. The patient's room is darkened and suggestion is employed. When the cervix does not dilate 15 grains of chloral and 40 grains sodium bromide are given by rectum, or gas and oxygen administered. It is important to obtain complete spontaneous dilatation of the cervix as slowly as possible; not only does the cervix dilate but the paracervical tissues retract which is most important and cannot be imitated by artificial means. When the head has left the cervix and rests between the levator and stretching the facia, ether is given to complete anesthesia and perineotomy is performed. The fetal heart sounds are carefully watched and forceps applied and patient delivered. Pituiglandol is often injected as the placenta passes out through the vulva, aseptic ergot is also injected if there is any hemorrhage. The operator waits five to ten minutes before delivering the placenta. If necessary the operator disinfects his gloves carefully and if the placenta is not visible inserts the left hand into the vagina and lower segment, palm up, while the uterus is pushed down on the placenta and the placenta then slides along the hand. If there is bleeding more pituitrin is given and $\frac{1}{4}$ grain of morphin and $\frac{1}{200}$ scopolamin is then administered to reduce the quantity of ether required for repair work, prolonging narcosis for many hours postpartum and abolish the memory of the labor as much

as possible. The cervix is then repaired and also the perineum and pelvic floor. The writer illustrates his conception of the anatomy of the parts and when this paper was presented, employed models to illustrate his idea. For this method the writer claims that it saves the woman the debilitating effects of suffering in the first stage and the physical labor of the second stage; but little blood is lost by this procedure. This method preserves the integrity of the pelvic floor and other tissues and prevents the results which follow lacerations. The brain of the child is protected from injury and from the effects of prolonged compression. In the hands of those not expert, this method might produce bad results. In a mother infected before labor complications might arise. The writer has had no mortality; mothers and children have done well. It is interesting to note that the method of version at the end of the first stage of labor proposed by Potter of Buffalo is condemned by the writer. He states while in Potter's hands the operation of version is safe, in less skilful hands very bad results will follow. In his mind, however, the same argument applies with less force to his recommendation of the operation of prophylactic forceps. This paper was presented before the American Gynecological Society and the majority of opinion was strongly against the adoption of this method in all cases and by all those who practise obstetrics. It was recognized as a procedure appropriate for experienced operators only.

Cranial and Intracranial Birth Injury.—Baily (*Am. Jour. Obst.*, October, 1920, No. 1) calls attention to the fact that a considerable proportion of stillbirths and early deaths are due to injury to the head of the child. In a few instances the prompt application of treatment might lower the mortality and morbidity. The mechanism of the injury has been described and illustrated. The veins of the cortex have little support as they enter the sinuses and hence pressure may readily rupture these vessels. In deformed pelves the head will mold unnaturally and undue pressure is inevitable. The posterior parietal bone may often produce severe injury. When the skull is fractured there is usually rupture of the meningeal vessels, although this condition seems to be rare probably because the dura is loosely attached to the bone in the newborn. A bad application of the forceps or excessive force might produce such a result. Bleeding from surfaces of the cortex is often retained beneath the pia and if near the cortical centers may produce considerable damage. Hemorrhage into one of the ventricles may occur from rupture of the coriplexus. The 40 cases proved by autopsy of cervical hemorrhage in infants, occurring at the Manhattan Maternity Hospital, are described in detail. Of these but 10 were not stillborn, 1 lived twenty minutes, another thirty, 1 three hours and others from fourteen hours to four days. But 2 of the children were delivered by forceps, 2 premature and 5 normal births. In the entire series 9 were forceps deliveries, 11 breech extraction, 5 preceded by version, 1 Cesarean case and 17 normal deliveries. The hemorrhage was diffuse in 18, especially marked under one bone in 11, diffuse, not in ventricle in 2, ventricle alone in 2, diffuse meningeal hemorrhage with thrombosis of the sinus in 1, 2 in the cerebellum, 2 in the pia mater, 2 in the dura mater. Five recent

cases of cranial and intracranial injury are reported in detail, three of them treated by operation with recovery and two dying without operation. In one of these a large osteoplastic flap was produced. In reviewing the literature of the subject it is found that results from decompression operations in infancy have not been really good. In some series the mortality has risen to 50 per cent. The raising of the depressed bone by piercing the bone with a sharp instrument and then pulling it up as recommended by Tweedy, is considered a makeshift.

American Journal of Obstetrics and Gynecology.—The publication so long issued by William Wood & Company, of New York, was by them discontinued some months previously. Obstetricians and gynecologists were not content, however, without a journal devoted exclusively to this branch of medicine. Dr. George W. Kosmak, editor of the *American Journal of Obstetrics*, with the assistance of others, formed an editorial board and the new journal was adopted as the official organ of the American Gynecological Association, American Association of Gynecologists and Obstetricians and Obstetrical Societies of New York, Philadelphia and Brooklny. It is edited by Dr. George W. Kosmak, of New York, with Dr. Hugo Ehrenfest, of St. Louis, as associate editor. The publication of the journal was assumed by the C. V. Mosby Company of St. Louis. The first issue of the journal is printed on good paper with clear type and illustrations well produced. With the endorsement of American obstetricians and gynecologists and under the control of its able editor and editorial board this journal should have a most successful career.

The Function of the Corpus Luteum.—OCHSNER (*Surg., Gynec. and Obst.*, November, 1920) contributes further observations upon the function of the corpus luteum. He quotes the observations of veterinarians and describes 9 cases among human beings, where he has operated and removed the false corpus luteum. The health of the patient was greatly benefited and in many cases sterility was relieved. He quotes 2 cases illustrating the importance of avoiding, in operations, injury to the true corpus luteum. Observations seem to show that such injury is followed by abortion. His investigations indicate that an unabsorbed false corpus luteum prevents ovulation and is a common cause of sterility and that when such a false corpus luteum is removed by excision or expression menstruation occurs as a result. While this is true of the false corpus luteum if the true corpus luteum is excised or ruptured during the early months of pregnancy, abortion follows and this must be considered as one of the common causes of early abortion. It is interesting to note that injury to the true or false corpus luteum may simulate ruptured ectopic gestation.

Abdominal Pregnancy with Living Fetus.—MAURY (*Surg., Gynec. and Obst.*, November, 1920) has collected 29 cases of abdominal pregnancy in which the fetus was living at the time of operation. These occurred between 1909 and 1918. In 62+ per cent. the diagnosis was made before operation. In the whole number 73 were operated upon, 55 recovered and 18 died, a mortality of 24.6 per cent. There

has been but little improvement in the maternal mortality in recent years and in fatal cases death resulted from hemorrhage, sepsis or both; embolism, pneumonia and intestinal obstruction were also causes of death. The infant mortality was between 40 and 50 per cent. In a number of cases the child was deformed (usually some form of talipes), and the rate of deformity was about one-third of all the children. This did not seem to result in congenital cases, but from pressure to which the child's limbs were subjected in its unnatural position within the abdomen. About one-fourth of them gave history of premature rupture while the remainder had not been diagnosticated. A great majority suffered from pain in the abdomen which sometimes caused nausea and vomiting and frequently produced faintness and syncope. In about one-fourth of the cases irregular bleeding from the uterus had occurred and in one patient menstruation had been regular up to the time of operation. The placenta was usually attached to the pelvic organs, in 2 cases to the liver. In some there was a pedicle which could be ligated like the pedicle of a cyst. In some cases the tissue was so situated that the placenta could be removed together with the organ to which it was attached. Statistics show that if the placenta can be completely removed the mortality is very much less than where it is left or partially removed. There is no constant statement concerning the size of the uterus which seems to have varied greatly in different patients. As regards treatment these patients may be divided into three classes: (1) Those where the condition is not recognized and the patient goes into spurious labor with failure to deliver herself; (2) those where diagnosis is made but where the patient is so comfortable that she prefers to go on to as near term as possible without operation; (3) those who suffer so much from pain, faintness, hemorrhage or toxemia that they seek medical aid and should receive operation at once. While the first class are most numerous, as they do not often come to the physician, they are of less practical interest than the third. The majority of medical opinion favors operation in abdominal pregnancy if possible during the life of the fetus. It has been found that the further the woman is from term the greater are her chances of developing serious complications, the first half of pregnancy is more dangerous than the second. In those patients who are fairly comfortable, if they are seen before seven and a half months, operation should be done in the interest of the mother, if they are seen after that time, if they are in good condition and doing well and can be kept under observation, operation may be deferred until the death of the child. In each individual case the operator must decide whether he will remove the placenta or allow it to remain. Complete removal has given a maternal mortality of 10 per cent. while the mortality has risen to 40 per cent. in cases where the placenta was allowed to remain. The decision, however, cannot be based on statistics alone, but each case must be examined and determined upon its individual merits. When a pedicle can be ligated, the removal is simple. When the placenta grows from an organ which can readily be removed, this is also favorable, but when the placenta has developed on the liver or mesentery or is plastered on the wall of the pelvis, decision is difficult and there is great danger of hemorrhage at the time of operation or subsequently.

HYGIENE AND PUBLIC HEALTH

UNDER THE CHARGE OF

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Lessons Taught by Measures for Control of Venereal Diseases.—PIERCE and WHITE (*Jour. Am. Med. Assn.*, 1920, lxxv, 1133) state that closer coöperation should be developed between state boards of health and the Public Health Service, and between state boards of health and local health officers to encourage a uniform method of venereal disease control throughout the United States. It adds much to the effectiveness of any public work to adopt and put into practice a uniform procedure. Uniformity impresses the fact on those that come into contact with the work that definite knowledge is possessed by health authorities. Health authorities should recognize the important part unofficial agencies may take in venereal disease control work if the activities of voluntary organizations are properly supervised. The moral, social and economic phases of venereal disease control work can be materially advanced by organizations and citizens interested in these particular problems. The results so secured will reduce the burden of the control of venereal diseases now largely borne by health officials. Progress will be materially advanced when the medical profession takes more interest in control of venereal disease than it does at the present time. Members of the medical profession should naturally assume leadership in all plans for promoting public health, and there certainly is urgent need for every physician to renew and maintain his interest in all phases of the present program for venereal disease control. Every medical college should provide better facilities for preparing future physicians to have a greater knowledge of the venereal diseases. There is need for a wider development of follow-up work in connection with treating persons infected with venereal diseases. A follow-up staff should be a part of the personnel of every venereal disease specialist. The duties of such a staff are to keep track of patients needing further treatment; to determine sources of infection; to see that precautions to prevent the spread of infections are being observed by patients; to discover other cases among the associates and members of the family of infected persons, and to carry on sociological and psychologic observations that will be of value in limiting the further spread of venereal infections. The question of equal treatment of both male and female infected persons must be placed on a scientific and equitable basis. *All* persons of either sex infected with either gonorrhea or syphilis are a very definite menace to the health of the community in which they reside; and unless infected individuals can be depended on to observe

precautions to prevent the spread of their infection to others, they should be placed under either modified or absolute quarantine restrictions. Careful and thoughtful consideration must be given by physicians, teachers, psychologists and intelligent parents to the question of deciding on the material to be used and the methods of applying instruction to questions of sex and venereal disease prevention. There is no phase of public health work which is attended by greater difficulties and which presents so many various aspects for consideration as does the problem of venereal disease control. Every one who has had actual experience in carrying on any part of the program has been greatly impressed with the tremendous scope and possibilities of the work and deeply realizes the necessity for not only continuing, but for greatly expanding the present plan of action. It can be stated without qualification or doubt that the great mass of intelligent citizens of the United States are deeply interested in this problem and will give their unqualified support to health officers, physicians and others attempting to meet their responsibilities for preventing the spread of venereal diseases.

An Epidemiological Study of an Endemic Focus of Leprosy.—Boyd and Fox (*Public Health Reports*, 1920, xxxv, 3007) have studied leprosy in a Gulf Coast city where the disease has prevailed for about thirty years. The investigation embraces 45 cases, at least 36 of which were infected locally. Males predominated, as in other leprosy foci. The age incidence showed the second decade to furnish more cases than any other, and residence in the focus of from eighteen to twenty years prior to onset was the rule. The tuberculous and mixed types formed the large majority of the cases. It is suggested that not all cases in the focus have come under observation. It seems likely that there are several fairly well-defined foci, other parts being relatively free. Persons of German birth or parentage seem especially susceptible. A history of contact with known lepers was obtained in about half of the cases. The possibility of insect transmission is discussed, but not regarded as likely. There is no official control of leprosy in the focus.

Information Concerning Rat Surveys and Rat Proofing.—The Public Health Service (*Public Health Reports*, 1920, xxxv, 2615) in this paper considers first the disadvantage of rat infestations from the economic, commercial and sanitary points of view, which is followed by a discussion of rat surveys for the detection of plague infection. The number of rats examined should be at least 1000 for every 10,000 of the human population, and a preliminary survey should be made in order that the most promising locations shall be trapped. The rat-proofing of buildings by elevation, to prevent harboring underneath, and by the use of concrete for floors and area walls is described, and model ordinances are presented.

Biological Investigation of California Rice Fields Relative to Mosquito Breeding.—Purdy (*Public Health Reports*, 1920, xxxv, 2556) made a study of the breeding of malaria-carrying mosquitoes in rice fields in California, contrasting the findings with those secured from a similar investigation in Arkansas. The most striking difference

was that while in Arkansas rice fields furnished many *anopheles* they furnished few or none in California. Indeed, no mosquitoes were found to breed in large numbers in the California rice fields. The author expresses the opinion that it is not practicable to control *anopheles* by control of the food supply of the larvæ on account of the diversity of organic matter, living or dead, which serves for the larvæ. The normal enemies of larvæ are described, particularly the top minnows (*Gambusia*) that have been so much used in mosquito control. The prevalence of the various mosquitoe found, and their seasonal distribution, are described.

The Role of Live Stock in Malaria Prophylaxis.—The U. S. Public Health Service (*Public Health Reports*, 1920, xxxv, 2462) quotes from ROUBAUD (original *Annales de l'Institut Pasteur*, 1920, vol. xxxiv) in reference to the possibility that domestic live stock may play a role in the prophylaxis of malaria. It has been noted in parts of western Europe that malaria may disappear without the extinction of malaria-carrying mosquitoes. It is asserted that in certain localities the *anopheles* prefer the blood of cattle, horses, etc., to that of man. It is proposed that advantage be taken of the habits of the *anopheles* and animal prophylaxis be made a part of the program of malaria control.

The Medical Profession and Notifiable Diseases.—BOWMAN (*Public Health Reports*, 1920, xxxv, 2503) details the reasons for requiring reports from medical men on the prevalence of certain diseases. He states that it is necessary to have compliance with the laws and rules on the subject in order that suitable control measures may be taken in the case of diseases that may be made the subject of sanitary control, and that in other cases the reporting is necessary to secure further knowledge of diseases about which we know too little now to be of practical value in their suppression. The following summary is presented: No disease has been placed on the notifiable list arbitrarily or by chance, but each for some definite reason. It therefore behooves every doctor to report every case of each notifiable disease for the following reasons: That the proper authorities may be informed and prevent further spread—That the information gained may be available as evidence of the need of public health work—That further knowledge may be gained as to the etiology and spread of diseases under conditions of which we now have no data—and That the location of areas where certain diseases prevail may be known when it is possible to undertake special measures for their eradication.

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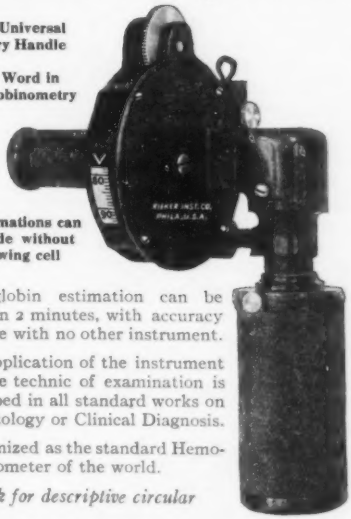

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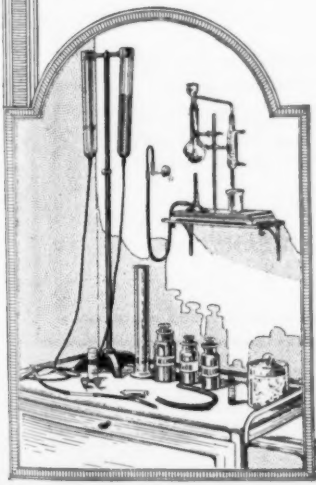

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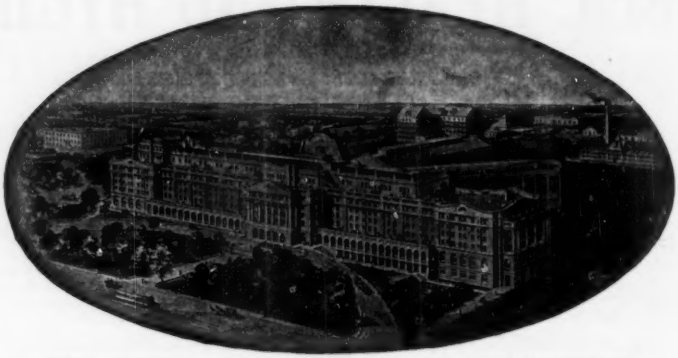

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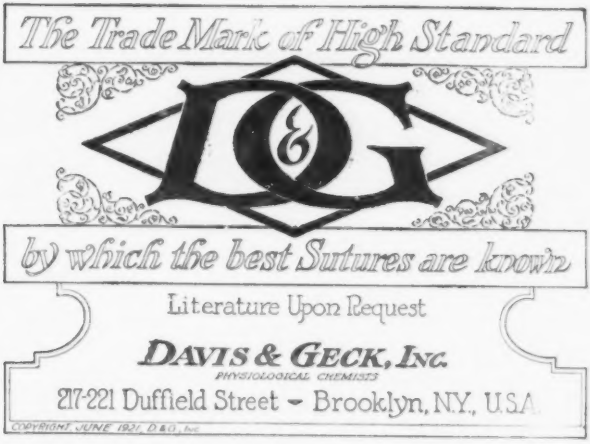
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